THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

OCTOBER, 1904.

ACUTE LEUKÆMIA IN EARLY LIFE.

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Acute leukæmia is a comparatively rare disease in early as well as in adult life, but with modern methods in blood examinations cases are now recognized more frequently than formerly. Morse,[1] in 1898, reported a case in a four-year-old girl and gave a brief résumé of seven other cases under ten years of age collected from the literature. McCrae,[2] in 1900, reported a three-year-old boy with leukæmia, giving abstracts of thirteen cases, including Morse's. Since McCrae's article I have collected fourteen cases, brief abstracts of which follow:

Case I. (Strauss.[3])—Boy, aged thirteen months; family and personal history good. Illness began two or three weeks ago, with enlargement of the abdomen. General condition good; no digestive disturbance; no nose-bleed. Physical examination showed marked pallor, slight rickets, numerous petechiæ, teeth good, tonsils normal, chest normal, spleen much enlarged, urine negative. Continued thus for two or three days, then became worse, and died three weeks from onset.

Blood. Hæmoglobin, 25 per cent.; erythrocytes, 2,008,000; leukocytes, 208,000; lymphocytes, 97.3 per cent.; large mononuclears, 0.6 per cent.; lymphocytes varying in size. Some poikilocytosis and polychromatophilia; few normoblasts.

Case II. (Bloch and Hirschfeld.[4])—Boy, aged eight months; family and personal history unknown. For a few days had been unusually sleepy; no other symptoms. Physical examination showed marked anæmia, right-sided pneumonia, lymph glands and spleen enlarged, rickets. Under observation for a few days, then had double pneumonia, and died.

Blood. No total white count given, but proportion of whites to reds was 1 to 12. Polynuclears, 28 per cent.; myelocytes, 10.2 per cent.; small mononuclears, 27.14 per cent.; large mononuclears, 38.8 per cent.; poikilocytosis, megaloblasts, and normoblasts; eosinophiles and mast-cells rare. Duration unknown, but probably acute. Regarded as lymphatic myelogenous type; autopsy showed leukæmic changes, especially interesting on account of changes in central nervous system.

CASE III. (Janeway.[5])—Boy, aged six years. Trouble began three months ago with swelling over masseters, later swelling of cervical and other glands, and marked pallor; no hemorrhage and no retinitis.

Blood. Hæmoglobin, 40 per cent.; leukocytes, 219,000; large lymphocytes, 87 per cent.; small lymphocytes, 11 per cent. Clinically, the case was chronic, but the blood was that of the acute type, and the author cites the case to show the impossibility of regarding acute lymphatic leukæmia as a separate disease.

CASE IV. (Jewett.[6])—Boy, aged thirteen months, smaller and weaker of twins. Family history negative. Personal history: never robust.

March, 1900. Pale, occasional diarrhœa, malnutrition. April: Slight, irregular fever. May: Tumor in left abdomen. Never any enlargement of superficial lymph glands; never any hemorrhages.

Examination. June: Moderate emaciation, pale, spleen much enlarged, reaching to level of umbilicus.

Blood. Hæmoglobin, 30 per cent.; erythrocytes, 1,912,000; leukocytes, 21,000; lymphocytes, 87 per cent.; neutrophiles, 10.5 per cent.; eosinophiles, 1.5 per cent.; myelocytes, 1 per cent.; eight normoblasts and eight megaloblasts in 200 cells; lymphocytes of all sizes; poikilocytosis and polychromatophilia; fever marked; regarded as subacute lymphatic leukæmia. Death, June 17th. No autopsy.

CASE V. (Jewett.[6])—Girl, aged seven months. Family history negative. For three months pallor, enlarged spleen, emaciation, diarrhœa, irregular fever, great weakness, enlarged glands. No hemorrhages.

Blood. Hæmoglobin, 20 per cent.; erythrocytes, 1,150,000; leukocytes, 33,000; lymphocytes, large and small, 78.6 per cent.; neutrophiles, 18.2 per cent.; eosinophiles, 1.8 per cent.; myelocytes, 1.4 per cent.; fourteen normoblasts in 500 cells. Death at eight months. Diagnosis: subacute lymphatic leukæmia. No autopsy.

CASE VI. (Pollman.[7])—Girl, newly born. Family history negative. Mother's blood normal. Sickly at birth, never cried nor nursed, apathetic, petechiæ on forehead and lower limbs, later universal. At sixteen days cyanosis; liver and spleen much enlarged; cervical and inguinal glands somewhat enlarged; temperature from 38.8° to 41.5° C. Death at nineteen days.

Blood. Erythrocytes, 2,500,000; leukocytes, 312,500. No differential count, but leukocytes, almost all mononuclear, with rather a large nucleus. Autopsy: great enlargement of spleen and liver and thymus, *open ductus arteriosus.* Tricuspid endocarditis. Culture from spleen negative. Culture from heart blood showed only colony of undetermined organisms. General infiltration of tissues with leukocytes. No examination of bone-marrow. Regarded as a case of splenomedullary leukæmia, but probably was lymphocytic.

CASE VII. (Stewart and Campbell.[8])—Boy, aged six years. Family history negative. Caught cold in March, 1901, never well afterward. Pallor, poor appetite.

Examination. April 1, 1901. Pale, submaxillary glands enlarged. Seen several times during April and May. Irregular temperature, nose-bleed, pain in legs. Spleen not enlarged.

Blood, May 26, 1901. Hæmoglobin, 21 per cent.; erythrocytes, 750,000. After large hemorrhages: leukocytes, 40,000; lymphocytes, 25 per cent.; polynuclears, 45 per cent.; myelocytes, 27 per cent.; eosinophiles, 3 per cent.; normoblasts fairly numerous. Death two days later.

CASE VIII. (Einhorn.[9])—Girl, aged nine years. Family history not mentioned. Well until several months ago, then weakness, later diarrhœa.

Examination. Not pale, cervical and inguinal glands enlarged, spleen and liver enlarged, chest negative.

Blood. Erythrocytes, 3,360,000; leukocytes, 389,000; small lymphocytes, 48.7 per cent.; large lymphocytes, 49 per cent.; mononuclears, 1.3 per cent.; polynuclears, 1 per cent. No further history given.

CASE IX. (Rocaz.[10])—Boy, aged four years. Came to hospital with tonsillitis, no diphtheria bacilli. Family history good. Previous history: subject to sore-throat. May 25, 1901, ill three days with tonsillitis, which subsided, but temperature remained high. In two days fetid diarrhœa.

Examination. Chest normal, tonsils enlarged, spleen enlarged. Widal reaction positive; case therefore regarded as typhoid. Four days later cervical and inguinal glands enlarged.

Blood. Hæmoglobin, 30 per cent.; erythrocytes, 1,816,000; leukocytes, 244,000; lymphocytes, 96.6 per cent.; large mononuclears, 0.6 per cent.; transitional, 0.6 per cent.; polynuclears, 2.4 per cent. Some poikilocytosis, later petechiæ, bleeding of gums. Death twenty-seven days after onset. Autopsy: hypertrophied thymus, infiltration of tissues generally with small cells.

CASE X. (Fowler.[11])—Girl, aged five years. Family history good. Previous history: measles, whooping-cough, chicken-pox. Two months ago sore throat, enlargement of cervical glands, pale, no appetite, no pain, weak. One month, hard swelling in abdomen.

Examination. Pale; tonsils enlarged, mouth breather. Chest: soft bruit at apex of heart; superficial glands slightly enlarged, spleen and liver much enlarged; retinitis (right); urine negative. Never any hemorrhages; temperature elevated.

Blood. Erythrocytes, 2,700,000; leukocytes, 240,000 to 250,000; small lymphocytes, 7 to 13 per cent.; large lymphocytes, 32 to 56 per cent.; polynuclears, 16 to 22 per cent.; myelocytes, 12.1 to 27 per cent.; eosinophiles, 0.6 to 2.6 per cent.; eosinophilic myelocytes, 0.7 to 3.4 per cent.; mast-cells, 0.3 to 4.4 per cent.; normoblasts numerous. Regarded as intermediate between lymphatic and myelogenous leukæmia. Died at four and one-half months after onset.

CASE XI. (McCaw.[12])—Infant, aged twenty months. Family and personal history good. Three weeks ago began to walk feebly and stagger, drowsy, and apathetic. Two weeks ago swelling of glands in neck, enlargement of abdomen.

Examination. Not pale, though hæmoglobin 38 per cent. Glands in neck, axillæ, and groin enlarged; spleen much enlarged; liver enlarged. Urine: albumin, oxalic acid crystals.

Blood. Leukocytes, 810,000; lymphocytes, 99.2 per cent.; later petechiæ and once blood in bowel movement. Spleen and glands diminished in size. Died about six weeks after onset.

CASE XII. (Taylor.[13])—Boy, aged ten years. Six weeks ago pain in legs, thirsty, yawning, enlargement of parotid and submaxillary glands, of liver, and left kidney.

Blood. Leukocytes, 15,000; lymphocytes, 46 per cent. A few days later leukocytes, 50,000; lymphocytes, 94 per cent., with increase in size of glands. Hemorrhage from mucous membranes. Died twelve weeks after onset. Autopsy showed general lymphatic infiltration.

CASE XIII. (Geissler and Japha.[14])—Boy, aged five years. Family history negative. Previous history, chicken-pox. Two months before became ill with fever, pain and swelling of abdomen, pain in feet, and later in all joints, general weakness; symptoms persistent ever since.

Examination. Well nourished, no rickets, chest negative, abdomen negative; urine negative; no swelling of joints nor pain on movement; no exanthem; slight enlargement of submaxillary and inguinal glands.

Blood. Hæmoglobin, 55 per cent.; erythrocytes, 2,200,000; leukocytes, 18,800; lymphocytes, 80 per cent. A few normoblasts, no poikilocytosis. Later petechiæ, nose-bleed, great enlargement of spleen and liver, no glandular swelling, increasing bone pains. Blood during the next three months ranged as follows: hæmoglobin, 22 to 60 per cent.; erythrocytes, 158,000 (after a nose-bleed) to 2,208,000; leukocytes, 12,000 to 34,150; polynuclears, 3 to 24 per cent.; mononuclears, 76 to 97 per cent. Poikilocytosis, many

megaloblasts temporarily after severe hemorrhages, many megalocytes in groups and about four times as large as a red corpuscle. A few neutrophilic and eosinophilic mastzellen, polychromatophilia. Death about five months after onset. Case at first might have been regarded as one of subacute rheumatism had it not been for the blood examination.

CASE XIV. (Glinski.[15])—Boy, aged one year. No family history. No previous history. For indefinite time pallor, malnutrition, vomiting and diarrhœa; prominence of eyes.

Examination. Pale, poorly nourished, submaxillary and cervical glands enlarged; bronchopneumonia on both sides; heart weak; spleen enlarged and hard; liver not enlarged; marked exophthalmus.

Blood. Hæmoglobin, 21 per cent.; erythrocytes, 918,750; leukocytes, 180,416; lymphocytes, 94.4 per cent.; neutrophiles, 5.3 per cent.; a few myelocytes and nucleated reds. Died with symptoms of pneumonia and heart failure. Autopsy, widespread leukæmic changes, especially in pia mater.

There can be no doubt of the diagnosis of leukæmia in any of the above cases. In all but Cases II., IV., and V. the blood count settles it beyond question. In Case II. there is no doubt of a marked leukocytosis, even though no total white count is given, the proportion of white to red being 1 to 12. The differential count was probably modified by the pneumonia, for we find 28.8 per cent. of polymorphonuclears, a high proportion for leukæmia. The total mononuclears, 60 per cent., would not be high for an eight months' infant in health, but is rather high for a leukæmia with 10 per cent. of myelocytes, and, together with this percentage of the last-named cell, justifies classing the case as one of the mixed-cell variety. Finally, the diagnosis is clinched by finding at autopsy typical leukæmic changes. As to Cases IV. and V., the advocates of von Jaksch's anæmia as a distinct disease might possibly class them as such; but I cannot recognize that anæmia as a distinct and separate disease, as a primary anæmia. It is secondary, the result of a variety of causes, chief among which are rachitis, syphilis, and severe intestinal disturbances. There is nothing in the reports of these cases to lead one to class them as secondary anæmia, while the leukocyte counts of 21,000 and 33,000, with the lymphocyte counts of 87 and 78 per cent. justify the diagnosis of lymphocytic leukæmia. That such comparatively low counts do occur in leukæmia is evidenced by Case XII. above, where were found at first a total count of 15,000, a lymphocyte count of 46 per cent., which figures a few days later had increased to 50,000 and 94 per cent., respectively.

My own case, now to be given in detail, also shows how low the total count may go. The history of this case, attended by Dr. John W. Fletcher, of Winnetka, and myself is as follows:

September 1, 1903. A. B., aged four years.

Family History. Maternal great-grandmother and paternal grand aunt died of phthisis. Father had trouble with ankle in infancy, said to be tubercular; outgrew it apparently, but for two or three years before birth of patient had more trouble with same ankle, though an exact diagnosis was never made. Two brothers, aged seven and nine years respectively, are well, but not robust, the former having adenoids. Sister, two months old, apparently healthy.

Previous History. Well at birth. Breast exclusively for three weeks; then breast and modified milk until seven or eight months, when weaned. General health has always been good, except that at times since early infancy the skin has shown marked pallor. An attack of acute tonsillitis in December, 1902. Has had none of the acute diseases of childhood. Appetite has been good, as a rule. Bowels generally regular, occasionally constipated.

Present Illness. For two or three months patient has had little appetite, and has shown a gradually increasing waxy pallor. There have been absolutely no other symptoms. The diet has been deficient in all directions, though more especially in the matter of fats and proteids. He has been up and about, out doors playing, has slept well, has not been fretful, bowels have been regular. In a word, except for his loss of appetite and great pallor, he has seemed perfectly well.

I first saw him professionally on September 1, 1903, at which time the result of the physical examination was as follows:

Physical Examination. Development and nourishment excellent, marked waxy pallor of skin and mucous membranes, shotty feel to cervical glands, both tonsils enlarged. Chest: area of cardiac dulness normal; apex, fourth space just inside mammillary line. Heart sounds strong and vigorous; soft systolic murmur heard generally over præcordia, but loudest at the apex; no bruit in neck. Pulse 96, regular, good strength. Lungs negative. Abdomen negative. No signs of hemorrhage anywhere; no tenderness over long bones. Blood: erythrocytes, 3,500,000; leukocytes, 10,000; hæmoglobin, 75 per cent. (Tallquist).

Directions were given to increase his diet in all directions, and he was given liquor potassi arsenitis in gradually increasing doses.

September 9th. Urine, 400 c.c.; specific gravity, 1021; no albumin, no sugar. Sediment: slight excess of leukocytes, a few renal cells, a very few normal blood corpuscles.

15th. Eats more under compulsion, but is no better; weight, forty pounds. Urine: specific gravity, 1020; no albumin, no sugar. No excess of indican. Sediment as before.

17th. Patient more easily tired, and is fretful. Physical examination: pallor is more marked, petechiæ present on neck, trunk, and limbs; not numerous; noticed by mother two days ago. Numerous black-and-blue spots in various places. No tenderness over the bones. Chest as before. Abdomen: spleen is felt one

inch by one inch below the ribs. Liver not enlarged, no distention. Blood (see table). Diagnosis: lymphatic leukæmia.

20*th*. Seen in consultation with Dr. Frank Billings, who concurred in the physical examination as reported above and in the diagnosis. Blood (see table).

21*st*. Ten c.c. of blood withdrawn from the median basilic vein by Dr. Ludwig Hektoen, who subsequently reported presence of the streptococcus.

22*d*. Sixty c.c. of human blood serum withdrawn yesterday from a vigorous woman were injected into the patient at 9.30 A.M. At the suggestion of Dr. Fletcher *x*-ray exposures were begun at 5.30 P.M. under the direction of Dr. W. A. Pusey. Blood (see table). Temperature, same.

23*d*. Much pain and discomfort from the serum injection. A few petechiæ. Blood (see table).

24*th*. Temperature higher, otherwise condition the same. Daily salt enema begun.

25*th*. Blood (see table).

26*th*. Spleen not felt and apparently not enlarged on percussion. Pulse between 132 and 134, strong and regular during the day, irregular during the night. Heart action strong and regular; murmur more intense and heard everywhere over cardiac area; some twitching of limbs; involuntary bowel movement at 8 P.M. Patient is decidedly worse. Blood (see table).

27*th*. Blood in bowel movements to-day for the first time; general condition same as yesterday.

28*th*. Much worse this morning; at times irrational and mildly delirious. More blood in bowel movements; pulse weaker, respiration becoming irregular. Oxygen started at noon—ten minutes, every twenty minutes.

29*th*. Moribund at 9 A.M. Unconscious and Cheyne-Stokes respiration at 10 A.M. Gradually sank, and died at 2 P.M.

Date.	Hæmoglobin.	Red.	Leukocytes.	Mononuclears.	Polymorphonuclears.	Eosinophiles.
September 1, 1903 . .	75 %	3,500,000	10,000	.....	.....	.....
" 16, " . . .	50 %	.....	Much increased.	99.5	0.5	.....
" 18, " . . .	45 %	3,116,000	30,000	98.9	1 0	0.1
" 20, " . . .	40 %	2,740,000	52,000	99.5	0.5	0.2
" 22, " . . .	40 %	1,892,000	80,020			
" 23, " . . .	.....	2,174,000	80,080	99.0	0.13	0.07
" 25, " . . . 5 P. M.	25 %	1,516,000	20.040			
" 26, " . . . 4.30 P. M.	20 %	1,544,000	6,300	98.2 1000 cells 1 myelocyte?	1.55	0.3 1 normoblast.
" 28, " . . . 4 P. M.	15 %	1,280,000	8,000			

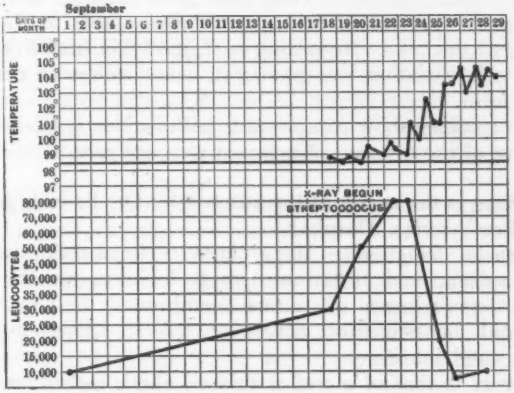
This case presents some points of extreme interest. First as to his heredity, the question of tuberculosis must be considered. The history of this trouble, three generations back, can have but little bearing on the case. The exact character of the trouble in the father's ankle apparently never was determined. On the whole, it is not probable that the tubercular taint played any part in the development of the child's final sickness.

When did this final trouble begin? This it is impossible to say. I saw the child frequently in a non-professional way throughout his life, and at times noticed his great pallor. Generally, however, he seemed perfectly well, so I said nothing to the family about his off days. His parents regarded him as the most robust one of three children. During the early part of last summer I noticed the increasing pallor, which was so great in early September that I then examined the child, with the result already detailed. There is no doubt in my mind that the malady began as early as last June or July, if not before. It is not at all improbable that the periods of intense pallor first noticed in infancy were in reality the beginning of his trouble. This, however, is pure speculation.

The absence on September 1st of all physical signs except the waxy pallor, enlarged tonsils, and condition of the blood is striking. The absence of hemorrhages until late in the disease is also quite remarkable. The presence of a few normal red blood corpuscles in the urine in the first examination may of course be regarded as a hemorrhage due to the leukæmic condition. The corpuscles, however, were very few in number, not more than one often sees in the urine of less serious conditions. There never was any nose-bleed, never any bleeding from the gums, and not until September 15th, two weeks before death, were any hemorrhages noticed under the skin. Indeed, the general absence of symptoms, except the pallor, were frequently commented upon by the parents. It was not until the onset of the acute symptoms with rapidly rising temperature, about six or seven days before death, that the child seemed acutely ill. It is unfortunate that I have not a record of his temperature during the first two weeks of September, but as he was up and out doors running around, the temperature was not taken. The three days' normal temperature, when systematic readings were first instituted, makes it probable that up to that time the temperature had been normal. I can but believe that the last week of illness simply marked the final acute stage of a chronic process which began months, possibly two or three years, before.

The chief interest of the case, of course, centres in the condition of the blood, especially in the leukocytes. The course of the erythrocytes, as a whole, shows a steady downward trend throughout the period of observation. That of the leukocytes is most interesting. (See chart.) Beginning with a normal count at the first examination, it rises rapidly during the first two weeks to 30,000, then still

more rapidly, reaching its maximum (80,000) five days later, when after two days more we see an ante-mortem drop to a point even subnormal—6300. The leukæmic agent, whatever it is, apparently was in the ascendancy during the first three weeks, and as a result of its action upon the bone-marrow a rapidly increasing leukocytosis takes place. Then, under influences indefinite and unknown, the upward march is checked, and is followed by a rapid descent. It is possible that the fall in this case was due to the presence of streptococci found in the blood on September 21st. The organism, of course, may have been present before this date. This was our first bacteriological examination of the blood. The next day the leukocyte count reached its maximum, and the day after that began to drop. At about this time also the temperature began to rise rapidly. It looks as though these two phenomena, rapidly rising temperature and rapidly falling leukocytes, might be due to the invasion



by the streptococcus. The leukæmic agent, however, is still active, the lymphocytes registering 98.2 per cent. and the polymorphonuclears 1.5 per cent. in a total white count of 6300. What the differential count at the first examination was I do not know, as unfortunately I did not examine any dry cover-slips, the total white count being practically normal. The next examination, however, two weeks later, showed the great increase, 99 per cent., in the mononuclear elements, which characterized the blood condition up to the time of death, and this condition may have been present on September 1st. It simply shows that in these severe cases of anæmia we must not be content with a total white count alone, but must study our dry specimens.

Study of the dried smears prepared with the Wright stain shows interesting blood pictures. The mononuclear cells resemble in structure lymphocytes having a round or slightly indented nucleus

that nearly fills the cell and takes a deep stain. A remarkable number of basophilic granulations are seen. There is great variation in the size of these mononuclears, the diameter ranging from six to thirteen microns, yet the small variety prevails. It is probable that both large and small cells have a common origin, and that the various sizes and shapes are due to violence in manipulation, for the size and appearance of the cells vary in different parts of the same specimen, those in areas where the layer of blood is thick, and where, therefore, they are protected from pressure in the process of spreading, being small and deeply stained; whereas, in areas where the smears are thin, and where, therefore, pressure is greatest, they are larger and less deeply stained, suggesting spherical lymphocytes that have been flattened out. Again, the edges of the larger forms are often uneven and ragged; the cell protoplasm is usually undemonstrable, as if the ectosarc had ruptured, leaving only the round nucleus. That such great changes were brought about by the process of smearing is attributable to the extreme friability of the cells. According to Capps* this friability and consequent cell variation are greater in acute leukæmia than in the chronic form.

Red corpuscles show considerable poikilocytosis, increasing with the course of the disease. Nucleated reds are rare.

Following is the report of the autopsy by Dr. Bassoe, pathologist at the Presbyterian Hospital:

Anatomical Diagnosis. Hyperplasia of intra-abdominal lymph glands, spleen, and intestinal lymph follicles; general anæmia; multiple hemorrhages of serous membranes, kidneys, myocardium, and bone-marrow; accessory spleen; agonal intussusceptions of small intestine.

The body is that of a well-nourished child, rather large for his age. The skin is very white. The external lymph glands are not enlarged. The peritoneal cavity is empty and free from adhesions. The pleural cavities are both empty, and there are no adhesions. The pericardial cavity contains a few cm. of clear fluid. The thymus is about 4½ cm. long by 2 cm. wide and 1 cm. thick. The tissue is very pale. Each lateral lobe of the thyroid measures 2½ x 1½ cm.; on section it is pale, grayish-red, and glistening. The mucous membrane of the larynx and trachea is smooth and extremely pale. The tracheal and bronchial glands are moderately enlarged, the largest being 18 x 10 x 3 mm., dark red externally and on section.

The weight of the left lung is 105 grams. The pleura is mottled, light gray and red, with small ecchymoses here and there. It crepitates throughout. The section is very pale and grayish-white. The

* Oral communication.

weight of the right lung is 125 grams, and is in the same condition as the left.

In the heart the epicardium is covered with a large number of ecchymoses. The tricuspid admits three finger-tips, the mitral admits one readily. The valve shows no changes. There are a few ecchymoses in the epicardium of both ventricles and the right auricle. The foramen ovale is closed, the myocardium is light-gray brown generally, but dark-red areas are seen throughout the entire thickness of the ventricular walls. The weight is 100 grams.

The spleen is smooth and weighs 90 grams. It measures 11 x 6 x 3½ cm. On section it is dark red, mottled with whitish bands and dots. At hilum an accessory spleen 1 cm. in diameter. The aorta is smooth. The pharynx was not examined. The œsophagus is smooth. The membrane of the stomach is smooth, with numerous reddish areas which do not disappear readily on pressure.

In the small intestine there are six descending agonal intussusceptions. The mucous membrane of the duodenum is pale and bile-stained, with solitary follicles enlarged. Peyer's patches are of a dark-grayish color and prominent, at about the ileocæcal valve is a patch 5 cm. long occupying the entire circumference. The appendix is 8 cm. long, and the lining is smooth. The solitary follicles are prominent throughout. In the sigmoid are a few blood-stained crusts.

The liver is 565 grams in weight, and smooth externally. On section it is a light grayish-brown in color, and but little blood exudes on pressure. The lobular markings are invisible, and the cut surface is of a homogeneous appearance. The gall-bladder contains fluid bile and the lining is smooth. The pancreas is of normal size and extremely pale. The adrenals are small and pale. The kidneys weigh 130 grams. The left measures 8½ x 5 x 3 cm. The capsule is not adherent and leaves a pale-gray surface, on which are a large number of ecchymoses, the largest measuring 6 mm. in diameter. On section it is extremely pale, the pyramids are white entirely, and the cortex markings can be made out in places. The section also has an area of small ecchymoses. There is a narrow reddish line between the pyramids and the cortex. The capsule is thin. The right kidney is the same size and contains a small amount of yellow fat. Otherwise it is the same as the left. The ureters are small. The bladder is extremely pale.

Lymph Glands. The retroperitoneal glands are moderately enlarged, the largest being 12 mm. in length and very dark. On section it is mottled grayish-red, and in places almost black. Those about the pancreas are the largest, the periaortic glands are of similar appearance. The mesenteric glands are uniformly prominent and dark red in color, but smaller. Cervical, axillary, and inguinal glands are not enlarged, but the iliac glands are slightly so.

The marrow of the sternum is of the usual deep-red color. The

marrow of the femur is also very red, with darker hemorrhagic foci.

The brain was not examined.

The meninges of the cord are very pale. The cord is preserved intact.

Microscopic. Heart Muscle. The section shows in several places infiltrating hemorrhage into the myocardium. The muscle fibres are forced wide apart by the blood. The number of leukocytes does not seem to exceed much the normal. A large per cent. are of the small mononuclear variety, with deeply staining nuclei. In parts of the section containing no hemorrhage the muscle appears normal.

Right Lung. In the upper lobe areas are found in which the alveoli are filled with a granular material containing many leukocytes. Between these areas there are areas showing compensatory emphysema. In the first-mentioned areas the walls of the alveoli are somewhat thickened, but not greatly congested. There is a noticeable increase in the nuclei in the walls. The leukocytes within the alveoli vary in kind. There are small mononuclear and polymorphonuclear and large mononuclear and polynuclear epithelioid cells, some of which contain pigment granules, also some cells which look like plasma cells. The epithelium of the bronchi is not in good condition, but it is in most cases found broken up within the lumina.

Left Lung. Lower lobe presents similar changes.

Liver. The liver cells are small and vacuolated, as if they were the seat of fatty degeneration. The spaces between the cords of cells are filled with a granular material. The interlobular vessels are surrounded by connective tissue, which is infiltrated with cells. The intralobular veins appear small. In the one large vein are many cells which have the same appearance as the surrounding liver cells. In one place a small lobule, surrounded by abundant connective tissue, gives the appearance of a cirrhotic liver.

Kidney. The vessels contain but little blood. The glomeruli show some increase in the number of nuclei, and there are some with ragged outline, and masses of cells with granular material in Bowman's capsule. The capsule is not thickened.

Convoluted Tubules. The cells are indistinct in outline, and here and there is found a cell within the tubule. The lumen is filled with granular material. The outlines of the straight tubule are in many cases made up of the basement membrane, with epithelial cells scattered within the lumen. Other tubules appear normal. The connective tissue shows no increase, but in many places is packed with leukocytes.

Pancreas. The pancreas shows very marked necrotic changes, which seem post-mortem in origin.

Spleen. The spleen presents in the section a mottled appearance, due to areas infiltrated with blood, alternating with areas contain-

ing little blood. This makes the Malpighian corpuscles for the most part hard to distinguish. The mottled appearance of the section gives it somewhat the appearance of a section of hæmolymph gland. In the hemorrhagic areas it is difficult to tell whether the nucleated areas seen are the pulp cells or leukocytes brought by the blood. The stroma is not to be seen in these areas. There are a few polymorphonuclear leukocytes.

Thyroid. The thyroid contains a moderate amount of colloid, occurring in masses separated from the walls of the acini by a large space. The epithelium is found desquamated in most of the acini and lying in the space surrounding the colloid. In many cases the acinus is entirely filled with small epithelioid cells, and there is an extensive cell infiltration throughout. On one edge of the section is a large quantity of pigment, probably the remains of hemorrhage. The suprarenal shows little change. The stomach contains areas of hemorrhage in the superficial layer of the mucosa, otherwise it appears normal.

Small Intestine. The mucous membrane is necrotic, and throughout nearly the whole length of the section, which is longitudinal, the submucosa is infiltrated with lymphoid cells. Near the muscularis these cells are somewhat far apart. Nearer the lumen they are densely packed, and at the surface they have undergone necrosis, and, with the remains of the mucous membrane, form the lining of the lumen.

Section through a Peyer's Patch. The mucosa shows the same change as in the other section. The centre of the individual follicles of the patch contain lymphoid cells, widely separated by granular material containing elongated irregular nuclei. The surrounding lymphoid cells are more densely packed, then become more loosely distributed for some distance in the submucosa. Near the lumen they show necrotic changes, as described in the other section.

Thymus. The organ is large, and the section shows remarkably little change from the infantile type. The corpuscles of Hassal are large, with blue-staining (hæmatoxylin) centres in many cases. It is lobulated, in the infantile form, but the lobules show no differentiation into cortex and medulla. The lobules are well filled with lymphadenoid cells. Many cells similar to these are found in the connective-tissue septa, and a few in the corpuscles of Hassal.

Accessory Spleen. The section shows the characteristic splenic capsule, with trabeculæ penetrating the gland. The parenchyma has the same structure as described in connection with the spleen.

Lymph Gland. The arrangement into lymph cords and channels is not very plainly marked, the lymph cords being so thin and containing relatively few lymphadenoid cells. Around the periphery of the gland the lymphadenoid cells are more abundant. The lymph channels contain many cells of the endothelioid type. These

are almost as numerous as the large and small lymphocytes. The number of cells in the channels is not more than normal.

Hæmolymph Glands (Retroperitoneal). Here the well-filled cords of lymph cells stand out in marked contrast to the blood-filled sinuses. The gland is of the splenic type. The circular sinus is very well made out in most of the periphery. Contrary to the usual finding, the central blood sinuses are packed with blood. This blood contains very many small mononuclear leukocytes, and also large mononuclear leukocytes. A few of what appear to be nucleated red cells are present, but there is no certainty of the identity of these, as there are many lymphocytes containing a minimum amount of cytoplasm surrounded by red cells. No hæmolysins could be made out with certainty, but very pale outlines of corpuscles with granular masses surrounding them, the granules staining as hæmoglobin, indicate some hæmolysis. There is little phagocytosis. In another gland the destruction of red cells is more plainly indicated. The spinal cord was negative; cultures therefrom were sterile.

Bone-marrow. The bone-marrow from the shaft of the femur and that from the sternum, in contrast to the normal, appear very similar. The marrow of the shaft of the femur shows little of the normal narrow reticulum surrounding fat vacuoles. Most of the vacuoles are absent, and the space is all occupied by a reticulum filled with blood containing large numbers of nucleated red cells(?). There are but few giant cells present. In most places the red cells are disintegrated into a granular material. There appear to be some nucleated red cells present, but, as in the hæmolymph glands, these cannot be made out with certainty.

The marrow from the sternum presents a similar appearance, but there are not so many red cells present, and the structure is more plainly made out. There are a few myelocytes present.

Bouillon emulsions were made from the lung, liver, spleen, and bone-marrow, and from these glycerin-agar slants were inoculated. No results after seventy-two hours. From the heart's blood the streptococcus was obtained in pure culture. The bile was sterile.

Study of this excellent report of Drs. Bassoe and Dick shows only what has been observed in previous cases. There are noted in organs and tissues generally the infiltration with lymph-adenoid cells, closely resembling the small mononuclear lymphocytes seen in the blood during life, showing the widespread distribution of these elements. The involvement of the bone-marrow is confirmatory of the views of Neumann and others, that no case of leukæmia thoroughly studied has failed to show an abnormal condition of this structure. Cultures from the bone-marrow, however, were negative. The presence of streptococci in the blood both during life and post-mortem observed in this case has also

been noted in other instances. The enlargement of the thymus noted here has also been observed by Rocaz. It is to be regretted that through an oversight no animal inoculations were made.

Morse's report of 8 cases, McCrae's of 6, and my own of 15 now give us 29 cases of acute leukæmia for study. It must be confessed, however, that their analysis adds little to our knowledge of the condition. There seems to be nothing in family or previous history which can be regarded as predisposing to the disease. The family history of tuberculosis in my own case led me to look up this point in others, Unfortunately such history is given in comparatively few instances. In 105 cases 51 make no mention of family history at all, and of the remaining 54 cases 41 are negative, and 14, or 26 per cent., have a family history of tuberculosis. Susmann,[16] studying the relation of leukæmia and tuberculosis, even concludes that a certain antagonism exists between the two conditions. The leukæmic condition improves, the total leukocyte count diminishing, the neutrophiles increasing. Following this hint injections of tuberculin have been tried in a few cases, but nothing conclusive has been determined thereby. It is not probable from the data available that tuberculosis plays a part either direct or indirect in the cause of the condition.

As to direct heredity, there have been reported only two cases of the condition in parent and child, too few from which to draw any conclusions.

As with heredity, so with the previous history of cases, nothing appears to act as a predisposing cause, except, possibly, chronic tonsillitis. A large proportion of cases show this condition, but here the question arises whether the tonsillar condition is not the result rather than the cause of the process. It is not improbable, however, that the infectious agents found in the late stages of leukæmia gain access to the system *via* the tonsils, and that to this extent at least the diseased condition of the latter may contribute to the final outcome.

No age is exempt. Leukæmia has been observed in the newborn child, and as late in life as seventy-one years.

The onset may be sudden, but more often is insidious, with vague indefinite symptoms, which gradually develop into the typical leukæmic picture.

The general course of the disease in children, on the whole, is the same as in adults, and is always fatal. It occurs more frequently in males, 21 of the 29 cases being boys. The spleen was enlarged in all cases, the liver generally, though the enlargement of neither was great. A not infrequent phenomenon was a diminution in the size of the spleen before death. General glandular enlargement was by no means constant, the cervical glands being most frequently involved.

The duration of the cases was from four and a half days to five

months. Six, possibly seven, of the cases were prolonged beyond the conventional nine weeks. The onset, however, is usually so insidious that it is impossible to determine exactly when a case does begin. Hence the impossibility of drawing a hard-and-fast line—*e.g.*, at nine weeks as the limit for acute cases. The acute part of the disease is undoubtedly but the final stage of a chronic process, the exact beginning of which we cannot determine.

Nor does the duration depend upon the type of the disease. The most prolonged case, five months, was lymphocytic, whereas the one myelocytic case lasted about two and a half months; and of the two mixed cases one died at the end of four and a half months, the duration of the other was unknown, but was probably short. (Case II.)

As in the adult, the chief interest in leukæmia centres in the blood. There is, of course, the diminution in erythrocytes and hæmoglobin. The lowest red count recorded is 750,000, and this was after severe hemorrhages. The leukocyte counts ranged from 6000 to 810,000. Several low counts have been observed, and always just before death. A falling white count, as in my own case, is apparently indicative of approaching death. Age apparently has no effect upon the total white count; thus of two thirteen-months-old children one had a count of 21,000, and the other 208,000, and the highest count, 810,000, occurred in a twenty-months-old infant.

The differential count showed that of the 29 cases 25 were of the lymphocytic type, 1 myelocytic (Case VII.), 2 of the mixed-cell variety (Cases II. and X.), and 1 case undetermined. The preponderance of the lymphocytic type is thus emphasized anew. The lymphocytosis, furthermore, is more apt to be of the small variety; this cell predominated in 12 cases, the large cell in 3, the two varieties equal in 2, and in the other cases no attempt is made to distinguish between them. The degree to which the lymphocytosis may rise is shown in my own case, where were found constantly 99 and 99½ per cent. of lymphocytes. The degenerated granular character which these cells may undergo is also well illustrated in the same case.

The polymorphonuclears are always reduced, often to an extreme degree. Thus in one specimen from my own case I counted 1100 cells before finding a neutrophile; in the same specimen also but one eosinophile was seen. The total count here being 80,080, the absolute number of each variety in a cubic millimetre of blood was as follows:

Mononuclears	79,919.8
Polynuclears	80.1
Eosinophiles	80.1
	80,080.0

Whatever the function performed by the neutrophiles, obviously it could not be carried on properly by such a small number of cells.

Except in the myelocytic and mixed cases, myelocytes were rarely present, and then only in small numbers. Nucleated reds were also rare, though found occasionally, especially in young subjects; thus case IV., thirteen months old, showed eight normoblasts and eight megaloblasts in a count of 200 cells, a striking example of the tendency of the blood in infancy to revert to the fetal type under pathological conditions.

Certain minor differences in the behavior of the disease in early life are observed. Thus, in children hemorrhages are apparently less frequent and less severe; in the 29 cases hemorrhage occurred in only 17, and in only 1 of these was it severe. It occurs in the nose, mouth, bowels, kidneys, and skin. The blood picture also represents a greater variety than in adults, and the lymphocytosis is more apt to be of the small type.

In an explanation of the abnormal blood picture, of this turning upside down of the different varieties of leukocytes, lies the solution of the whole leukæmic problem. The change is undoubtedly the result of a chemotactic agent acting upon the bone-marrow, the clinical manifestations and type of disease depending upon the nature of this chemotactic agent whatever it may be. Of the real nature of this agent and of its action upon the bone-marrow we know nothing.

The diagnosis of leukæmia can be made only by a complete examination of the blood. Profound anæmia and leukocytosis are so frequent and arise from such a variety of causes in infancy and childhood, that there is more chance of error in early life unless one makes a differential white count, the only means by which a diagnosis can be clinched. In the absence of marked symptoms a constant and comparatively high lymphocytic count (90 per cent.) must be observed, owing to the great ease with which a lymphocytosis is set up at this time. Thus I was somewhat disturbed once at finding in a pale twenty-two-months-old infant with hypertrophied tonsils, adenoids, and enlarged cervical glands, a white count of 20,000 and 70 per cent. of lymphocytes. Subsequent examinations, however, showed a normal condition of the blood. Conversely a leukæmia with marked throat symptoms may be mistaken for an ordinary acute infection. There is little danger of confusing leukæmia with pertussis.

The effect of intercurrent disease or infection upon leukæmia is interesting. This subject has been carefully studied by Dock[17] and others, and in a general way it may be said that there is almost always a fall in the total leukocytes, and also, though less uniformly, there is a disposition for the leukæmic character of the blood to disappear more or less completely and for the polynuclear to in-

crease absolutely as well as relatively. The total leukocytes have been known to fall as low as 471. Case II. in my own series, for example, shows the effect of a double pneumonia in an eight-months-old boy; we find 28 per cent. of polynuclears and 65 per cent. of total mononuclears. The influence of tuberculosis has already been mentioned. Dock's study shows the effect of influenza, erysipelas, acute and chronic tuberculosis, abscess, etc.

Turning now to the pathological side of the question, the results of autopsies do not throw much light on the problem. Post-mortem examinations in adults and children have shown the widespread distribution of the disease, abnormal appearances having been found in practically all organs and tissues of the body. The condition found most commonly has been an excessive infiltration of tissues with small mononuclear lymphoid cells, identical in appearance with the smaller lymphocytes with which the circulating blood is flooded during life.

Perhaps the most important contributions which have been made to the pathology of the subject are those which have shown that the bone-marrow *only* need be involved in order to produce the disease, whether of the myelocytic or lymphocytic type. For the researches of Neumann, Walz, Pappenheim, Brandenberg,[18] Kelly,[19] Reed[20] and others have shown that the bone-marrow is *always* involved, the glandular system sometimes not at all, sometimes only slightly, as in my own case; and they maintain that no case which has been thoroughly studied has failed to show a pathological condition of the bone-marrow. The incorrectness of the terms "lymphatic" and "myelogenous" is thus obvious. All cases are "myelogenous"—*i. e.*, of bone-marrow origin. The terms "myelocytic" and lymphocytic," suggested by Kelly and others, are preferable for the present, even though they are based on a physical sign, *i. e.*, on the presence of either myelocytes or an excess of lymphocytes in the circulating blood.

The description of the bone-marrow given in my own case is typical of the changes found in this tissue. These changes are not always found in all parts of the bone-marrow. They may be localized, and are found most commonly in the shafts of the long bones.

The comparatively few bacteriological investigations which have been made are of a negative value. Streptococci and staphylococci have been found in the blood during life, also these and other familiar organisms have been found in the blood and tissues post-mortem, but no specific organism which can be considered as causing the condition. It is probable, furthermore, that these organisms are secondary invaders. Nichols[21] found in 92 cases showing bacteria that in chronic leukæmia organisms were found oftener in the terminal than in the earlier stages. They are probably the result rather than the cause of the original underlying processes, and, as already mentioned, the frequent occurrence of

hypertrophied tonsils in leukæmic cases suggest that they may have gained access to the system by this route.

Thus, lacking knowledge as to the exact cause of leukæmia, various theories have naturally been advanced to explain the disease. Nichols[21] has studied these various theories, grouping them under three heads: (*a*) toxic, (*b*) infectious, and (*c*) cancerous or hyperplastic. Of these only the infectious theory has been studied experimentally, and the results here have been negative. Discussing the cancerous theory, he likens the enormous number of leukocytes in leukæmia to the proliferation of epithelial and connective-tissue cells seen in carcinoma. He finally concludes that until the true nature of leukæmia is understood both the toxic and cancerous theories must be considered among the possible causes of the disease.

Nichols' paper is exhaustive and valuable, but study of it and leukæmic literature generally suggests the desirability of further investigations in two directions: injections of blood from living leukæmic patients directly into the bone-marrow of animals, and, secondly, injections of pure cultures of various pathogenic organisms into the same structure. As far as I have been able to learn from a pretty careful review of the literature, such investigations have not been carried out with pathogenic organisms at all, with leukæmic blood but once, and then with a negative result. Accepting as we must the bone-marrow as the primary pathological lesion of the condition, our efforts should be directed toward ascertaining the nature of the agent producing that marrow change. Fascinating and absorbing as is the study of leukæmic blood, the condition found there represents, after all, only one physical sign of the disease. The real question is, *why* do the bone-marrow and the other blood-making organs produce this kind of blood, *what* is the agent causing the organs to manufacture 99 per cent. of lymphocytes instead of 40 per cent., or to set free in the circulation 27 per cent. of myelocytes instead of an occasional one?

Treatment is of no avail. Arsenic is generally given, but is useless. The record of cases treated with the *x*-ray thus far gives no promise of permanent help. The hope that such treatment may be of service is based presumably on the theory that leukæmia is a malignant disease of the bone-marrow. Granting the truth of this there is less chance of the improvement seen in more superficial malignant disease, owing to the fact that calcium salts offer greater resistance to the passage of *x*-rays than do other constituents of the body; hence the greater difficulty of affecting bone-marrow.

The natural behavior of leukæmia in patients attacked with an intercurrent disease, suggests a method of treatment not hitherto tried to any extent. If the fall in total leukocytes, the attempt to resume a normal leukocyte formula, and the reduction in splenic enlargement, phenomena already mentioned, in reality be due

to the newly invading agent, it seems not unreasonable to hope that injections of sera, anti-streptococcic, anti-pneumococcic, etc., might accomplish the same result, and thus bring about an amelioration of the most prominent pathological conditions of the disease. True, no case thus complicated has ever recovered, nor has tuberculin been of permanent value; still in a disease as obscure and as uniformly fatal as is leukæmia, any methods of treatment are justifiable. Sera injections seem worthy of trial.

CONCLUSIONS. All cases of leukæmia are myelogenous in origin. As in adults, the acute variety is more apt to be of the lymphocytic type.

The disease is rare in early as well as in later life. It is probably more common than has been supposed, however, 22 cases of the acute or subacute variety having been reported since 1898, while previous to that date only 7 cases are on record.

The course in children differs from the adult type only in minor details; hemorrhages are fewer and less severe, the lymphocytosis is more apt to be of the small variety. The disease is always fatal.

It is suggested to use injections of sera in treatment.

Experimental inoculations with leukæmic blood and with cultures of pathogenic organisms are desirable, such inoculations to be directly into the bone-marrow.

I am much indebted to Professor Hektoen, Drs. Bassoe and Dick for the thorough pathological report, and to Dr. Joseph A. Capps for valuable help in the examination of the blood.

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A CASE OF ACUTE LYMPHATIC LEUKÆMIA.

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At the beginning of the nineteenth century pallor of the blood, as if mixed with pus, was observed by Bichat. This appearance combined with enlargement of the spleen was observed by Velpeau[1] in 1827. The alteration in the blood depending on an excess of leukocytes Donne described and interpreted in 1844 as due to imperfect transformation of white into red blood cells.

In October, 1845, Hughes Bennett and Dr. Craigie[2] published two cases of the disease, and to the former appears to belong the credit of recognizing the salient features of the affection as a distinct malady. In November, 1845, Virchow[3] published another case independently and admirably worked out.

In all these cases the change in the blood was only recognized after death. Virchow proposed the name leukæmia and Bennett leukocythemia. It was first observed during life by Dr. H. M. Fuller in 1846 and subsequently by Dr. Walshe.

In 1848 the first case during life was diagnosed by Vogel. Ebstein,[4] in reporting several cases, calls attention to the fact that traumatism may play an important role in the etiology. A. Fraenkel,[5] in organs from a case of leukæmia, pointed out that there was present a lymphoid infiltration, especially of the kidney. Herman Suchannek[6] found in the nasal mucous membrane that the olfactory epithelium was normal, but that the glandular structure was destroyed by the infiltration of lymphocytes. Monro[7] cites a case of leukæmia in which there were found on histological examination numerous small oval bodies in the heart, between the fibres, smaller than nuclei of leukocytes, and too irregular in size to be regarded as bacteria. They were not present in any other organ. Grewe[8] reports a case of acute lymphatic leukæmia following a strain in lifting a weight, in which the blood was characteristic of lymphatic leukæmia. At autopsy, the lymph glands were enlarged, spleen hypertrophied, and the liver and kidneys contained lymphoid nodules. Palma[9] reports a case of primary sarcoma of the thymus with secondary deposits in the lymph glands. A month later the patient showed an increase in the number of leukocytes and Palma concluded it to be a case of lymphatic leukæmia preceded by pseudo-leukæmia. Dock[10] mentions a case of chloroma, which condition

was most marked in the periosteum in and about the orbit, and numerous widespread metastatic nodules, all of a pea-green color. The polynuclear leukocytes averaged 20 per cent., the small lymphocytes 7 per cent., and the large lymphocytes 65 per cent. Normoblasts occurred in the proportion of two to five per thousand of red corpuscles. Only one eosinophile could be found "out of many thousand leukocytes counted."

Fraenkel believed that the large lymphocytes could be regarded as pathognomonic of acute lymphatic leukæmia. Hirschloff reported two cases of leukæmia in which most of the leukocytes were large mononuclear cells without granules; some, however, contained neutrophilic and some eosinophilic granules. According to Birch-Hirschfeld and Benda the variation in size may have an anatomical basis in the hyperplastic lymph nodes, as in some cases these contain mostly small lymphocytes. Müller claims that myelocytes (both neutrophilic and eosinophilic) and mast-cells are usually absent or extremely scarce in leukæmia. Polynuclear leukocytes (both neutrophilic and eosinophilic) are also comparatively scarce. Nucleated reds are usually very scanty and may not be found at all, according to Ewing.[11] Intercurrent affections may greatly alter the appearance of the blood in leukæmia. Fraenkel cites a case in which the leukocytes fell from 220,000 to 1200, and ascribes it to a pure leukocytolysis. After typhoid fever, pneumonia, empyema, erysipelas, septicæmia, tuberculosis, and carcinoma the same changes have been noted.

Kraus recently reported a case in which the leukocytes fell from 393,000 to 4000 as the result of double pneumonia and empyema. The viscera showed no evidence of leukæmic infiltration and he inferred that the infection had not only transformed the blood, but had resolved the essential visceral lesions as well.

After the subsidence of the infection, the blood soon resumes its original condition, according to Grawitz. The reduction of leukocytes can also be accomplished by experiment, as in a case cited by Jacob, which showed 850,000 reduced to 282,000 by the injection of glycerin extract of spleen. Richter obtained the same results by injecting spermin; and Henck[12] by injection of tuberculin. Kinnicutt[13] reports a large number of eosinophiles in the blood in a case of leukæmia. Nobl[14] regards the mitoses of Müller as the only certain evidence of leukæmia. In two cases examined the eosinophiles were scanty. In Uthemann's[15] case 93 per cent. of the white cells were lymphocytes. According to Osler[16] eosinophiles and nucleated red corpuscles are rare and myelocytes are not present. Cafafy[17] claims that the amœboid movement of the white cells is feeble, due in all probability to the large number of mononuclear elements present. Of 16 cases of leukæmia reported by A. E. Taylor,[18] 12 presented an increase in the number and percentage of mast-cells. In the remaining 4 cases no mast-cells were demon-

strable. He stated that not one of the cases showed 4,000,000 red cells, and claimed that there was always an oligocythæmia present. He considers the condition to be due either to cachectic or nutritional disturbances, to toxic hemolysis, or to disturbances in the bone-marrow. Polychromatophilia and poikilocytosis are almost constant features in leukæmia. Nucleated red cells, most of which were normoblasts, were found in all but one case of the sixteen examined. Microblasts, macroblasts, and poikiloblasts were also present. The lymphocytes were devoid of movement, while the myelocytes showed constantly slight motility. As low a percentage as 15.6 of polymorphonuclear leukocytes was noticed in one case. Eosinophilia was not constantly present in lymphatic leukæmia, while it was invariably present in myelogenous leukæmia. Leukoblasts, according to Löwit, can be found in developmental areas in the lymph glands, spleen, intestines and bone-marrow in acute leukæmia. In but one case of lymphatic leukæmia were circulating mast-cells demonstrable. Fraenkel admits that myelocytes may occur in acute lymphatic leukæmia, and Benda claims they are frequently, if not constantly, found in the circulating blood and that local basophilia is very common in leukæmia.

Dunn[19] cites leukæmia in a child of eight years, in which there was a crescentic tumor in each upper eyelid. The first evidence of the disease was a swelling in the parotid gland, which increased greatly in size and became as hard as stone.

Middleton[20] contributes 2 cases of leukæmia, one a child of sixteen months, the other a boy four years old. In the first the proportion of leukocytes to erythrocytes was 1 to 9. Paris[21] cites a case of leukæmia in a boy of seventeen years which after six days terminated fatally. Post-mortem examination showed the typical lesions of leukæmia in the spleen and liver, but the lymphatic glands were wholly normal. Eichhorst[22] also mentions acute leukæmia in a lad of eight years; the duration of the disease, fourteen days.

Vesemeyer[23] reports 3 cases of acute leukæmia terminating in three, five, and ten days, respectively; Ortner,[24] a child eight and a half months old, and Ebstein[25] reports a case ending fatally six weeks after the patient first came under observation. Ord and Copeman[26] call attention to a case of five years' standing; Lannois[27] one of three years' duration.

Saenger[28] records the occurrence of lymphatic leukæmia in a pregnant woman in which premature labor had to be induced on account of unbearable distention from uterus and spleen. He also calls attention to a case of congenital leukæmia, the child being stillborn in the thirty-second week. The blood upon examination showed one white to three red blood cells. The mother's blood was not examined. Litten[29] reports acute lymphatic leukæmia following influenza that terminated in three days; Guttman, a

child of ten years, in which the ratio of white to red cells was 1 to 1¼, and that only a single eosinophile was observed in a preparation; Wertheim, in a case of lymphatic leukæmia, found no nucleated reds, the white corpuscles numbering 480,000. Thayer[30] mentions that nucleated red cells are rare, and if present are likely to be megaloblasts. Müller found very few eosinophiles in a case of lymphæmia; Thayer[31] found 0.1 per cent.

Wilkinson[32] reported a case of leukæmia which, upon first examination of the blood, showed 560,000 leukocytes, chiefly myelocytes. Eight days later a second examination was made, when it presented all the features of lymphatic leukæmia, while only an occasional myelocyte was observed. Nucleated red cells—normoblasts and megaloblasts—were present, the latter predominating. At the first examination of the blood so much polymorphism of the white cells existed that an accurate differential count could not be made. No necropsy was obtained.

Nichols[33] reports 2 cases of acute lymphatic leukæmia. In one the leukocytes numbered 67,800 per c.mm., "all of which excepting a small proportion were large lymphocytes." A second examination made three days later showed 134,800 leukocytes per c.mm., in which the large lymphocytes numbered 91.3 per cent. and small lymphocytes 7 per cent. In this case a coccus was present "differing from the ordinary known cocci" in the blood and organs, but produced no specific action when inoculated into guinea-pigs and rabbits. In another case the leukocytes numbered 529,000 per c.mm. Eighty-five per cent. of them were large lymphocytes, 10 per cent. small lymphocytes.

A. O. J. Kelly[34] cited 4 cases of acute lymphatic leukæmia. The first showed 17,000 to 30,000 leukocytes, 93 per cent. of which were lymphocytes; the second (a young woman who had been delivered of a child a short time before), where the leukocytes ranged from 200,000 to 400,000 and the lymphocytes constituting 98 per cent.; the third, a young man in whom sepsis was suspected, a differential count of the blood showed 98 per cent. lymphocytes; the fourth, a man whose spleen was enlarged, where the leukocytes varied from 12,000 to 38,000.

Kelly doubts the non-identity of the two varieties of leukæmia—myelogenous and lymphatic. He bases his doubts upon several conclusions: 1. The occurrence of cases of so-called acute lymphatic leukæmia, with little or no enlargement of the lymph glands. 2. The demonstration of the predominance of lymphadenoid changes in the bone-marrow in every case of lymphatic leukæmia in which the bone-marrow has been examined—observed by Neumann many years ago. 3. The fact that distinctions between the lymphocytes and the granulocytes are of degree rather than of nature, since the lymphocytes are unquestionably amœboid, some possess granules in their protoplasm, and there is some evidence

of the occurrence of an active lymphocytosis. 4. The fact that the lymphocytes and the granulocytes (myelocytes and the granular cells of the circulating blood) develop from a common ancestor in the bone-marrow—at least, in pathological states. 5. The fact that even clinically there is no sharp dividing line between the two forms of the disease.

Rather than two forms of the disease, there are extremes of type. That atypical and transitional (intermediate or mixed) forms do occur, and while we have hitherto thought that acute leukæmia is always lymphocytic and chronic leukæmia either lymphocytic or myelocytic, trustworthy evidence has recently accumulated tending to show that acute leukæmia may be, though rarely, myelocytic. Contrary to the rule, certain of the chronic lymphocytic cases reveal a usually large number of large lymphocytes, and some of the apparently acute cases may be of the small lymphocyte type.

Fraenkel,[35] reporting 10 cases of acute leukæmia, "drew particular attention to the blood picture which he considered typical for such cases. He describes the predominating cell as varying greatly in size from that of a red blood corpuscle to those twice as large and showing every grade of transition between the two. The large cells contain voluminous nuclei which nearly fill the cell, leaving only a narrow zone of protoplasm about them. The nuclei are round or oval, but many show indentations, and some are even polymorphous. The typical small lymphocytes are much less numerous than these large elements, but are still absolutely increased above the normal. He notes further the absence of myelocytes and eosinophiles and the relative and even absolute decrease in the number of polymorphonuclear neutrophiles."

Hamman[36] reports 3 cases of acute leukæmia in which there was an increase in the large mononuclear cells (hyaline(?) cells).

The counts of the leukocytes were in the first case 111,000, of which 77 per cent. were large mononuclear cells; in the second 119,200, of which an average of 74.4 per cent. were large mononuclears in two counts, while in the third there were 958,000 leukocytes with 90 per cent. large mononuclears. He claims that it appears unjust from the evidence at hand to relegate a blood picture as distinctive as that of Fraenkel to a subgroup under the lymphocytic variety.

In the absence of any definite pathological basis our only means of classifying leukæmias is according to the blood picture. Ehrlich was the first to adopt this method, but he uses the blood picture merely as a gauge to certain anatomical seats of the disease. Evidence being in favor of the absence of such an indication, it has been proposed to replace the terms myelogenous and lymphatic by the more uncompromising ones, myelocytic and lymphocytic, which have reference to the blood picture alone.

Savory,[37] in a child aged four and a half years, who presented enlarged glands of the axilla and above the right clavicle, found upon examining the blood 35 per cent. hæmoglobin, 2,157,000 red cells, and 356,000 leukocytes. Spreads of the blood stained with hæmatoxylin and eosin showed that the red cells were practically normal, and only found two nucleated red cells while counting 611 white cells. Both were normoblasts. A differential count of the leukocytes gave: polynuclears 3.45 per cent.; large and small lymphocytes, 96.07 per cent.; eosinophiles, 0.33 per cent.; myelocytes, 0.16 per cent. "The large lymphocytes greatly predominated, but there was no line of demarcation between the large and the small; so they were counted together. The majority seem about from 12 to 14μ in diameter." Death occurred in seven weeks. No autopsy was performed.

Zypkin[38] reports a case of a woman, aged thirty-nine, in whom a first examination of the blood showed the presence of 2,700,000 erythrocytes, 8800 leukocytes, and 35 per cent. hæmoglobin. At this examination the polynuclear leukocytes were 64.5 per cent.; large lymphocytes, 22.4 per cent.; small lymphocytes, 5.4 per cent.; mononuclear leukocytes with ungranulated protoplasm, 6.4 per cent., and eosinophiles, 1.3 per cent.

Two weeks later the erythrocytes were 1,550,000; leukocytes, 106,400; hæmoglobin, 24 per cent. In this report the large lymphocytes were 64.7 per cent.; polynuclears, 11.9 per cent.; small lymphocytes, 6.3 per cent.; mononuclear neutrophiles, 2.4 per cent.; mononuclear leukocytes with ungranulated protoplasm, 14.4 per cent.; eosinophiles, 0.3 per cent. Poikilocytes, normoblasts, and megaloblasts were present. In this case there was enlargement of the spleen—four fingers' breadth—below the border of the ribs, and the observer thinks that it was primarily a splenic anæmia in which a transition into acute lymphatic leukæmia occurred.

G. S. Middleton[39] reports a case of acute lymphatic leukæmia occurring in a youth nineteen years of age which proved fatal three months after the glandular enlargement was first noticed (cervical glands). The white blood cells, though not counted in a hæmocytometer, were estimated at about 30,000 per c.mm. Large lymphocytes were 87.3 per cent.; small lymphocytes, 4.2 per cent.; polymorphonuclears, 2.5 per cent.; large mononuclears (hyaline), 6 per cent. No marrow-cells or mast-cells were observed and extremely few eosinophile cells. The red corpuscles showed a moderate poikilocytosis, but no nucleated reds were found. The number of erythrocytes and the percentage of hæmoglobin were not estimated.

Puchberger[40] claims that in leukæmia there are observed markedly hypertrophic forms of blood platelets, which sometimes attain the size of lymphocytes. When the blood is stained with brilliant cresylene blue he noticed, after the lapse of ten or fifteen minutes, the separation of a hyaline substance which, in the form of a cylin-

der, is inseparably attached to the similarly circumscribed stained substance of the blood platelet.

Wende[41] mentions a very interesting case of lymphatic leukæmia preceded by Hodgkin's disease. There was spontaneous increase and reduction of tumors, characteristic of Hodgkin's disease, with suddenly developing clinical and blood changes showing transition from pseudoleukæmia into true lymphatic leukæmia. The first blood examination gave: hæmoglobin, 88 per cent.; erythrocytes, 5,128,000; leukocytes, 4000. Differential count: lymphocytes, small, 27 per cent.; lymphocytes, large and transitional, 4 per cent.; polynuclears, 68 per cent.; eosinophiles, 1 per cent. Microblasts and microcytes were occasionally observed.

Several months later two blood examinations gave a general result as follows: hæmoglobin, 40 per cent.; erythrocytes, 1,856,000; leukocytes, 39,000; lymphocytes, small, 95.4 per cent.; lymphocytes, large, 1.1 per cent.; eosinophiles, 0.5 per cent.; polynuclears, 2.9 per cent.; myelocytes, 0.1 per cent. Microcytes, macrocytes, and poikilocytes were observed, as well as an average of 168 nucleated reds (102 in first and 225 in second) per c.mm. and a number of polychromophiles.

A streptococcus infection occurred, and just twenty-four hours before death the hæmoglobin was 30 per cent.; erythrocytes, 803-000; leukocytes, 1600, and the specific gravity 1.030. Megalocytes and poikilocytes were found, together with schistocytes; no normoblasts. The small lymphocytes were 88 per cent.; large and transitional lymphocytes, 1 per cent.; polynuclear neutrophiles, 10 per cent.; eosinophiles, 1 per cent. Infiltration of lymphocytes was more or less marked in all the organs and in the skin.

Dorothy Reed[42] cites a case of a man, aged forty-seven years, in whom the disease was preceded by a severe attack of epistaxis. The blood was examined twice, ten days and seven days before death. An enormous increase in the leukocytes was apparent, the white cells being about as numerous as the erythrocytes. No differential count was made. No general or even local enlargement of the lymphatic glands was noticed; the bronchial, peritracheal, and aortic glands, though deeply pigmented, were rather soft and translucent. The mesenteric glands were not enlarged, were deeply pigmented, grayish-yellow and translucent, and somewhat softer than normal. Along the retroperitoneal region the hæmolymph glands were very conspicuous, had a dull-red color, and were not especially enlarged.

In blood smears made from the heart at autopsy in over a thousand non-granular mononuclear cells, only three or four granular polynuclear leukocytes and four normoblasts were seen. The uninuclear cells varied from cells almost twice the size to those considerably smaller than the normal red blood cells. The nuclei were round or oval. The red cells appeared normal in size, form,

and staining properties. Nucleated cells were of the normoblast type. Section of a chicken-fat clot from the heart showed a meshwork of fibrin and entangled leukocytes, the most conspicuous of which was the lymphoid cell. In the marrow the predominating white cell was the lymphocyte; few normoblasts, but no megaloblasts, were observed. In the lymphatic glands the sinuses were engorged with lymphocytes and the follicles to a less extent. All the viscera contained small foci of infiltration of lymphocytes, but none to a marked degree. Reed suggests that "there are three forms of leukæmia, all due to myelogenous changes, and that these should be known as the myelocytic, lymphoid, and mixed-cell varieties, if we wish to make the blood picture the basis for clinical divisions."

Miller and Hess[43] report a case of acute leukæmia with death due to rupture of the spleen. The leukocytes varied from 50,000 to 161,000. An average differential count gave: small lymphocytes, 4 per cent.; large lymphocytes, 81 per cent.; eosinophiles, 3 per cent.; myelocytes, 1.5 per cent., and polynuclears, 10.5 per cent. Numerous megaloblasts were observed.

Williams,[44] in speaking upon the pathology of leukæmia, claims that there are two forms: one in which the cells are derived from the marrow (myelocytic) and one in which the cells originate mainly in the lymph glands, though also found in smaller numbers in the spleen and marrow (lymphocytic). Lymphatic is a rarer disease than myelocytic leukæmia, and the primary affection is in the lymph glands. We find these glands enlarged, whitish or grayish-white on section, and overloaded with lymphocytes. Many are decidedly larger than usual, but all are of the same type. We never find any form of marrow cells or eosinophiles in pure lymphatic leukæmia. Secondary deposits of a similar character are regularly found in the spleen and marrow and sometimes in other organs. The blood is surcharged with lymphocytes, great and small. The primary disease—leukosis—is seated in the lymph glands.

Pawlowski[45] describes a bacillus in the blood and tissues, especially in the lymphatics and blood paths of the liver, in three cases of leukæmia. He infers that the leukæmia is the reaction of the leukocytes of the blood-forming organs and to a less extent of the blood itself to the irritant bacillus. Fermi isolated a short, blunt bacillus from the spleen of a person dead of leukæmia, but failed to find it in twelve spleens in persons dead of other diseases. Kelsch and Villard[46] found and proved the pathogenic properties of the bacillus (in rabbits) discovered by Fermi.

A. Westphal[47] reports a case of acute leukæmia in which death was precipitated by a puncture of the spleen made for diagnostic purposes. At the necropsy the spleen was enveloped with a large blood clot; no large vessels were ruptured. Cultures were made from all the internal organs and fluids with negative results.

Ord and Copeman[48] discovered Charcot-Leyden crystals in the blood of a leukæmic, both before and after death, but many more after death; Westphal[49] found the same crystals in fluid drawn from the spleen during life.

Von Jaksch[50] claims that peptone can be demonstrated in the blood where disintegration is marked, as in leukæmia.

Mathes, of Jena,[51] examined the blood of 2 cases of leukæmia for peptone and allied bodies. In neither did he find peptone, but in each deutero-albumoses were demonstrable in the blood and serum.

Xanthin and hypoxanthin are present in the blood, as well as lactic and formic acids, according to Strümpel.[52]

Freund and Obermayer[53] found a notable decrease of fixed substances and a notable quantity of peptone in the blood of leukæmic individuals. Upon chemical analysis the spleen yields xanthin, hypoxanthin, glutin, glycocoll, leucin, and tyrosin. The same authority (Roberts[54]) says there is an increase in the fat and fibrin in the blood, with albukalin, mucin, and acetic acid, together with xanthin, hypoxanthin, lactic and formic acids. Bohland and Schurz[55] have determined that the excretion of uric acid is increased in leukæmia. Toulmin[56] reports 2 cases of leukæmia in negroes, one being interesting on account of a malarial history and the disappearance of leukocytosis, with diminution in size of the spleen under treatment with arsenic. Quincke[57] and Stintzing both observed a recession of the symptoms of leukæmia after the onset of general miliary tuberculosis. Engelhardt of Riga[58] records a case in which there was an attack of hæmoglobinemia, hæmoglobinuria, and icterus.

The case of lymphatic leukæmia here reported came under the observation of Dr. Julius Salinger in the Jefferson Hospital in 1900, and to whom the writer is indebted for the clinical history of the case.

The clinical notes are: K. S., aged forty-eight years, female, white, married. Mother died of tuberculosis at the age of fifty-six; father died of apoplexy at fifty-four; one brother died of tuberculosis; three other brothers also deceased, causes unknown.

In childhood the patient had measles, mumps, scarlet fever, and two attacks of diphtheria; good recovery followed all these diseases. Menstruation was first noticed when twelve years of age. The periods were painless, the flow profuse, lasting from three to seven days. One child was born to her when she was thirty years of age, and she had no miscarriages. Six years ago she had peritonitis, the attack lasting two weeks, with eventual good recovery.

Six weeks before coming under observation the patient noticed dyspnœa on slight exertion. The attack of dyspnœa was followed by severe pain, more or less periodical. This pain (dull and gnawing) was limited to an area reaching from the lower margin of the last ribs to the anterior superior spine of the ilium on the left side. Relief was obtained by assuming the prone position and when

lying on the left side. Œdema of the arms and legs followed these attacks of pain, which condition persisted for several days, leaving her in a very much weakened condition. Headache, vertigo, and impairment of vision (as of a scum over the eyes) were also prominent symptoms. Bowels were constipated, tongue coated, appetite fair.

An examination of the sputum was negative as regards tubercle bacilli. Examination of the urine resulted as follows: color, lemon yellow, clear; specific gravity, 1010; reaction, acid; albumin, a trace; sugar, none; urea, 1 per cent. Microscopic examination showed oxalate of lime crystals, amorphous urates, and a few squamous epithelial cells. No casts were demonstrable.

Repeated examinations were made of the blood, and these are appended:

June 19, 1900.	Hæmoglobin	25 per cent.
	Erythrocytes	1,000,000
	Leukocytes	22,500
	No differential count made.	
June 20, 1900.	Hæmoglobin	25 "
	Erythrocytes	931,200
	Leukocytes	23,000
	Differential count of leukocytes was:	
	Small lymphocytes	62.5 "
	Large lymphocytes	3 "
	Polynuclears	32 "
	Eosinophiles	2.5 "
July 7, 1900.	Hæmoglobin	25 "
	Erythrocytes	1,000,000
	Leukocytes	2,500
	Differential count of leukocytes was:	
	Polynuclears	69 "
	Small lymphocytes	23 "
	Large lymphocytes	8 "
	Eosinophiles	0 "
July 13, 1900.	Hæmoglobin	25 "
	Erythrocytes	1,240,000
	Leukocytes	2,800
	Differential count of leukocytes was:	
	Polynuclears	70 "
	Small lymphocytes	22 "
	Large lymphocytes	8 "
	Eosinophiles	0 "
Aug. 10, 1900.	Hæmoglobin	40 "
	Erythrocytes	1,204,000
	Leukocytes	4,000
	Differential count of leukocytes was:	
	Polynuclears	63 "
	Small lymphocytes	26 "
	Large lymphocytes	10 "
	Eosinophiles	1 "
	Poikilocytosis was observed in this examination.	
Aug. 16, 1900.	Hæmoglobin	35 "
	Erythrocytes	1,782.000
	Leukocytes	111,000
	Differential count of leukocytes was:	
	Polynuclears	5 "
	Small lymphocytes	90 "
	Large lymphocytes	5 "
	Eosinophiles	0 "

Aug. 22, 1900.	Hæmoglobin	40 per cent.
	Erythrocytes	1,672,000
	Leukocytes	35,009
	Differential count of leukocytes was:	
	Polynuclears	7 "
	Small lymphocytes	92 "
	Large lymphocytes	0 "
	Eosinophiles	1 "
	This count shows poikilocytosis and nucleated red cells.	
Aug. 28, 1900.	Hæmoglobin	35 "
	Erythrocytes	1,796,000
	Leukocytes	16,000
	Differential count of leukocytes was:	
	Polynuclears	20 "
	Small lymphocytes	79 "
	Large lymphocytes	0 "
	Eosinophiles	1 "

As a result of the blood examination a diagnosis of lymphatic leukæmia was made. The patient did not improve under treatment, but gradually grew worse, and died.

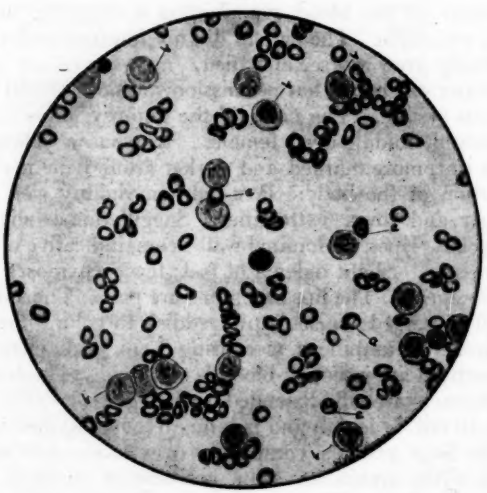
An autopsy was made, but permission was not granted to examine the nervous system. The notes of the autopsy follow: Body of a well-preserved, middle-aged female. Skin has a yellowish-brown or bronze tint, more marked and darker around the neck than any other portion of the body. Post-mortem rigidity well marked in both upper and lower extremities. Suggillation is slight in back and buttocks. Upon abdominal wall, scars, indicative of past pregnancy, are seen. Slight œdema of feet; few ecchymoses upon scalp near the forehead. The lips and gums are pale. The subcutaneous fat is well preserved; musculature reddish in color. Small epiplocele is present at umbilicus, measuring 3 cm. in diameter. Vessels of the omentum are injected; blood is still fluid. The larger vessels of the stomach are all distended and engorged. The appendix measures 10 cm. in length and is intimately bound down by mesentery. The liver extends completely over to the left side and to 5 cm. below the umbilicus. The peritoneum contains 100 c.c. of slightly cloudy fluid. The pericardium contains 100 c.c. of clear, straw-colored fluid; otherwise it is normal.

Right side of heart is dilated. The right auricle contains a large number of chicken-fat clots, together with a large quantity of fluid, watery blood. Right ventricle contains a few currant-jelly and chicken-fat clots and fluid blood; while the left auricle and left ventricle are comparatively empty. As the heart is cut from the great vessels a large number of small clots and a large quantity of blood wells out. Heart weighs 330 gms. Muscle is flabby, pale in areas, and there is an abundance of epicardial fat present. The right ventricular wall is thin, and the adipose tissue represents about two-thirds of its thickness. There is slight thickening of the tricuspid and mitral leaflets; aortic valve shows fenestration of middle leaflet; beginning atheroma of the aorta is also noticed.

Left pleura shows marked general adhesions; the lung is compressed and markedly œdematous. Weight 480 gms. Right pleura is universally adherent; the right lung is more œdematous than the left. Weight 570 gms. The spleen is large, dark red in color, measures 22 cm. by 17 cm. by 7 cm. The surface shows areas of capsulitis and the organ is adherent to the under surface of the liver. Upon section the organ cuts with slight resistance, and there is an apparent prominence of the Malpighian bodies; no amyloid reaction could be obtained. Weight 300 gms. The left adrenal shows no appreciable change macroscopically.

The left kidney is movable, enlarged, pale, and flabby, and measures 16 cm. by 3.5 cm. by 2.5 cm. and is slightly lobulated.

FIG. 1.



It cuts with some resistance. The organ is pale throughout; there is a slight increase of adipose tissue in the pelvis. The capsule strips with ease and the surface is smooth. Weight 180 gms.

The right adrenal is apparently normal.

The right kidney is also slightly movable, lobulated, flabby, and cuts with ease; the substance is pale. The capsule strips easily, leaving a smooth surface. Weight 170 gms. Both ureters are normal.

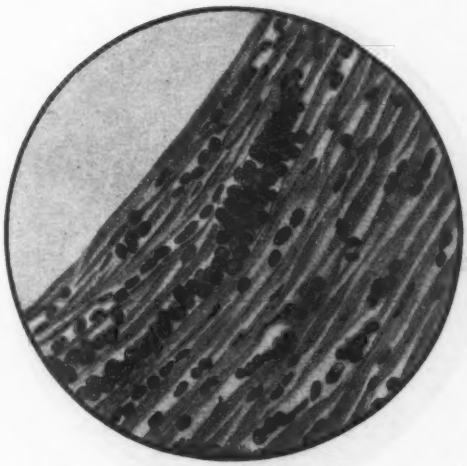
The liver, as mentioned previously, extends completely to the left side of the abdominal cavity. It measures 33 cm by 23 cm. by 9 cm. The organ is slightly paler in color than normal and cuts with slight resistance. Throughout the substance small, whitish or yellowish-white areas, more or less continuous with one another,

are seen, which do not give the amyloid reaction. The upper surface of the liver shows few areas of peritonitis. The gall-bladder is distended and contains 30 c.c. of a black, tenacious, tarry fluid. The bile-duct is patulous; no calculi in gall-bladder. Weight of liver 2800 gms.

Upon the under surface of this organ there is a large number of small masses, 1 to 5 cm. in diameter, which cut with slight resistance. Upon the cut surface (of these masses) small, pinkish-white, translucent areas 2 mm. in diameter are noticed, which do not give the amyloid reaction. These masses are apparently enlarged glands.

The uterus is normal; the left ovary is prolapsed and cystic; right ovary is atrophied. The bladder is empty and its walls are

FIG. 2.



very much thickened. The stomach is apparently normal and shows the usual congestion noticed post-mortem. The pancreas measures 18 cm. by 3 cm. by 1.5 cm., and is apparently normal. Weight 95 gms. The intestines present no apparent lesions macroscopically.

Histological Examination. The musculature of the heart is swollen and slightly granular. The striations in some fibres, as well as the nuclei, have disappeared. In some areas the muscle nuclei are normal, muscle fibres are wavy or spiral, and in still others fragmentation is present. The capillaries are filled with leukocytes, few of which are finely granular oxyphiles, but mostly lymphocytes. Irrespective of the capillaries, numerous lymphocytes are found between the muscular fibres, some in single, others in double column.

In one specimen a large accumulation of these cells is seen occupying the spaces of a fragmented fibre—*i. e.*, situated between the separated ends. In another specimen areas made up of a delicate, wavy, homogeneous tissue are seen, in which are entangled lymphocytes. These areas seem to have taken the place of heart muscle destroyed by fragmentation. Very few red blood corpuscles are demonstrable, either in the capillaries or between the fibres. Numerous mast-cells or mucinoblasts are also noticeable. Oil globules, both small and large, are seen in those specimens fixed with osmic acid. A large number of slightly oval and some spindle-shaped cells (these latter being finely granular and having no apparent nucleus) are also demonstrable, especially around the capillaries.

FIG. 3.

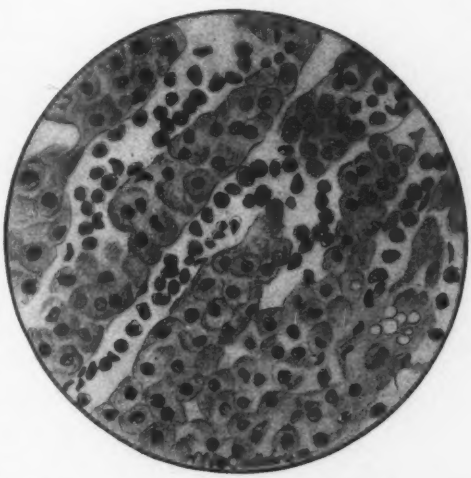
In examining the spleen the first thing that impresses the observer is the appearance of unusual cellular density of the sections. Enormous numbers of erythrocytes are seen scattered throughout; most of these are perfectly normal, exhibiting no fragmentation whatever. The bloodvessels are engorged, principally with leukocytes; some of the vessels show rupture of the coats, even those within the trabeculæ, while others show infiltration or dissection of the coats by lymphocytes. The whole splenic pulp seems to be made up of two cells—erythrocytes and lymphocytes. The Malpighian bodies are not at all prominent, and in some the small artery is infiltrated with the cells. Upon closer examination small masses of lymphocytes are seen, more or less cylindrical in shape, which correspond to leukæmic infarcts. Few mast-cells are demonstrable.

The capsule of the organ is thickened and, to some extent, infiltrated with lymphocytes, even to the extreme periphery. Despite the presence of such a large number of erythrocytes in the splenic pulp there is very little pigmentation present.

The cells of the adrenals are slightly cloudy or granular. The cortical portion of the organs are infiltrated with lymphocytes. This is most marked in the zona reticularis; the zona fasciculata shows some, while the zona glomerulosa shows the least infiltration. In the medullary portion there is no appreciable alteration. The small quantity of adipose tissue surrounding the adrenal is also infiltrated with lymphocytes.

The left and right kidney show cloudy swelling, the nuclei of some of the cells being distinctly visible, others showing an entire

FIG. 4.



absence of nuclei. The protoplasm is distinctly granular; in some tubules only granular débris is present. Large areas of cellular infiltration are noticeable between the tubules, and to some extent obliterating them. At first glance one might think it was an area of acute infection, but upon closer examination the cells are found to be for the most part lymphocytes. Together with these is a large number of slightly granular, spindle-shaped cells which resemble those found in the heart. Besides the large areas of cellular infiltration mentioned above, single and double columns of lymphocytes are seen between the collecting tubules. The capsule of Bowman is also infiltrated with lymphocytes.

The liver shows an extensive and marked cloudy swelling of the parenchyma, the nuclei being for the most part entirely obscured

or very faintly outlined. Between the columns of cells throughout the entire organ are lymphocytes which encroach to such a marked degree upon the liver substance that a certain amount is destroyed. Small and large aggregations of lymphocytes are seen (irrespective of those between the cells), some circular in outline and others irregular, which correspond to leukæmic infarcts. These are visible to the naked eye. There is a slight degree of fatty infiltration present, but no evidence of a cirrhotic process. Under a higher magnification the liver substance appears more or less in islands, and together with the lymphocytes mentioned quite a few red blood cells are seen between the rows of liver cells. Histologically the pancreas is comparatively normal, showing only a few lymphocytes around the bloodvessels.

FIG. 5.

Examination of the intestine shows marked lymphocytic infiltration between the crypts of Lieberkühn and in the villi. There is no evidence of ulceration, but the enormous number of lymphocytes resembles very closely areas of infection. In the submucous and muscular coats large numbers of mast-cells are demonstrable, especially in the former. There are also a few of these cells seen in the villi. The bloodvessels are dilated and filled with lymphocytes.

The peribronchial and mesenteric glands show such an increased density that the typical arrangement is destroyed. There is also a certain amount of pigmentation present in the former. Few mast-cells are demonstrable.

There is no apparent increase in the elastica in any of the organs examined.

The bone-marrow of the ribs is extremely pale and scant. The cancellated structure is distinctly dry. Spreads made from the marrow contain lymphocytes and a few red blood cells, the latter mostly in islands. An occasional myelocyte and hyaline cell are seen. A few nucleated red cells are demonstrable, some exhibiting extrusion of the nucleus.

Spreads made from the heart's blood, spleen, and liver show exactly the same cellular elements as those from the bone-marrow.

Some granules of the polynuclear leukocytes and lymphocytes give the iodophilic reaction.

FIG. 6.

Inoculations were made from the bone-marrow, liver, spleen, kidney, and blood upon agar, blood serum, blood-smeared agar, and acid agar. From the bone-marrow and blood a bacillus which resembled the bacillus coli communis, morphologically, tinctorially, and biologically, was obtained. From the liver no growth was demonstrable at the end of twenty-one days. From the spleen a diplococcus (which corresponded morphologically and tinctorially to the diplococcus of Sternberg) and the staphylococcus pyogenes aureus were isolated. From the kidney the bacillus pyocyaneus and staphylococcus pyogenes aureus were obtained.

The case is interesting on account of its rarity and the comparatively short duration of the illness. All the organs examined except the pancreas show the lymphocytic infiltration to a marked degree. The infiltration of the peribronchial glands and conse-

quent enlargement would, no doubt, account for the dyspnœa. The bacterial findings apparently indicate an agonal infection.

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EXPERIMENTAL ARTHRITIS AND ENDOCARDITIS PRODUCED BY A STREPTOCOCCUS ISOLATED FROM THE BLOOD OF A CASE OF RHEUMATISM, ENDOCARDITIS, AND CHOREA.[1]

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Although rheumatic fever is believed by many to be an acute infectious disease, the specific agent concerned in its causation has been widely disputed, and even at present few authorities are agreed as to its etiology. The symptomatology, the frequent association with endocarditis, and the unique character of the disease have always suggested that rheumatic fever was due to some bacterial infection, and, therefore, it is not surprising that most of the investigations regarding its etiology should be carried out with this thought in mind. The results of many of the earlier studies were confusing and often contradictory, but certain recent investigations, coming especially from Germany and England, seem to throw some light upon the problem.

The intimate relationship between chorea and rheumatism,[2] and the artificial production of chorea by intravenous inoculation of a diplococcus from a case of rheumatism, as claimed by Beattie, to be referred to later, makes this subject doubly interesting.

In much of the earlier work done by Sahli,[3] Singer,[4] and others cultures from the blood, urine, and joint fluid of cases of rheumatic fever frequently yielded not one but several types of bacteria. Among these staphylococci, streptococci, and even certain bacilli belonging to the colon group were described. Experimental inoculations proved the virulence of these bacteria, but arthritis and endocarditis could scarcely if ever be reproduced. Contradicting these observations were the results reported by Chvostek,[5] and Kraus,[6] who could not obtain any growth of bacteria in cultures from the blood, joint fluid, or urine. In 1897 Achalme[7] published

[1] Read before the Association of American Physicians, Washington, May 11, 1904.

[2] Lewis, Seasonal Relations of Chorea and Rheumatism, The American Journal of the Medical Sciences, September, 1892.

[3] Deut. Arch. f. klin. Med., 1892, Bd. li. p. 451.

[4] Aet. u. Klinik des akuten gelenk rheumatismus, 1898, Leipzig, Verhandl. des XIX. Cong. f. inner Med., 1901, p. 441; Wien. klin. Woch., 1901, No. 20.

[5] Wien. klin. Wochen., 1895, No. 26, p. 469.

[6] Zeit. f. Heilkunde, 1896, Bd. xvii.

[7] Annal de l'Inst. Pasteur, 1897, p. 845; Gaz. méd. de Paris, 1901, No. 14, p. 105.

an account of his work with a spore-bearing anaërobic bacillus which he had previously described in 1891. This organism was cultivated from the blood of cases dying of acute articular rheumatism. The bacillus grew best in milk. Inoculations into animals produced spreading hemorrhagic phlegmons and general septicæmia. The later work of Menzer and others goes to show, however, that this organism may be obtained from the bodies of cadavers or even from milk which is not overcarefully sterilized, the spores being very resistant to heat. Walker considers that this organism is bacillus enteritidis sporogenes.

Wassermann,[1] in 1899, described a diplococcus or streptococcus which he obtained in cultures from the heart's blood and endocardial vegetations of a child dead of rheumatism, endocarditis, and chorea. This diplococcus developed in the ordinary culture media exactly like streptococcus pyogenes, but produced the most remarkable lesions in animals. A series of successive intravenous inoculations into eighty rabbits showed that it was possible to set up a multiple arthritis which rarely proved fatal. The joint symptoms occurred with great regularity, and developed only after an incubation period of three to six days. Frequently the infection spread from one joint to another. Soon these results were confirmed by Triboulet,[2] in France, who was able to produce in some of his rabbits endocarditis, pericarditis, and pleurisy. Later, Menzer[3] and Meyer[4] obtained streptococci from the throats of patients suffering from rheumatic angina. These organisms were characterized principally by their power of producing multiple arthritis in rabbits. The joint lesions occurred constantly, and were often associated with a vegetative endocarditis. Singer[5] somewhat later announced that the streptococcus which he had previously described was identical with the organism obtained by these observers.

In England the extremely severe type of rheumatic fever has afforded an excellent field for the study of this disease, and the results obtained by English observers have, perhaps, been more striking than those reported from other countries. Poynton and Paine,[6] since their first publication, in 1900, have isolated a diplostreptococcus from twenty-two cases of rheumatic fever. The organism was obtained occasionally from the blood before death in severe cases, but usually from the blood, endocardial vegetations,

[1] Berl. klin. Wochen., 1899, No. 29, p. 638.

[2] Compt.-rend. de la Soc. de Biolog., 1898, v. p. 124; Gaz. des hôp. des Paris, 1902, t. lxxv. p. 1439; ibid., 1903, t. lxxvi. p. 405.

[3] Act. des akuten Gelenkrheumatismus, Berlin, 1902.

[4] Zeit. f. klin. Med., 1903, Bd. xlvi. p. 311; Verh. des XIX. Cong. f. inn. Med., 1901, p. 452; Verh. des Vereins f. inn. Med., January 7, 1901.

[5] Loc. cit.

[6] Lancet, 1900, vol. ii. p. 861; British Medical Journal, 1901, vol. ii. p. 779; Medical Press and Circular, 1903, vol. cxxvi. p. 478.

and complicating lesions after death. Intravenous inoculation into rabbits was followed by an interesting train of lesions. Monoarthritis and polyarthritis was an almost constant result, while endocarditis, pericarditis, and pleurisy were occasionally encountered. The organism could be cultivated from the joints and endocardial growths of the animals. Among other lesions subcutaneous fibroid nodules were described in which the particular diplococcus could be demonstrated. Definite chorea could never be reproduced in any of the animals. Poynton and Paine consider that this organism is identical with that described by Wassermann and Triboulet, and believe that it is the specific cause of rheumatic fever. Recently Ainley Walker[1] and Walker and Beaton[2] have fully confirmed Poynton and Paine's results. They were able to cultivate a diplococcus from fifteen cases, including acute rheumatism, rheumatic endocarditis, pericarditis, chorea, and endocarditis. Intravenous inoculations into animals produced monoarthritis and polyarthritis, pericarditis, endocarditis, septicæmia, and death. Beattie[3] claims to have produced chorea as well as endocarditis and arthritis in rabbits inoculated intravenously with a diplococcus obtained at autopsy from the knee-joint of a case of rheumatic fever. Finally, Shaw[4] has made a comparative study of the cocci isolated by Wassermann, Poynton and Paine, and Walker. He finds that these various bacteria produce practically the same effects when inoculated into rabbits and monkeys, and may give rise to endocarditis, pericarditis, myocarditis, arthritis, pleurisy, and iritis.

In America almost no work had been done on this subject. Dana,[5] in 1894, found diplococci in sections of the meninges of a child dead of chorea, but since cultures were not made the character of this organism must remain in doubt.

The recent papers of Poynton and Paine, Walker, and Menzer deal quite extensively with the literature upon the subject. In view of the interesting experiments which have been made in England and Germany it was thought advisable to record the following case of rheumatism, endocarditis, and chorea.

M. H., female, aged eight years, admitted into the Orthopædic Hospital and Infirmary on October 15, 1903, under the care of one of the writers, with the following history furnished by Dr. W. T. Skinner, of Glasgow, Delaware:

"Toward the latter part of August or early part of September, 1903, the child was taken sick; she had fever and was confined to bed with a swollen and painful ankle. Under salicylate of soda

[1] Practitioner, 1903, vol. lxx. p. 185.
[2] British Medical Journal, 1903, vol. i. p. 237; ibid., vol. ii. p. 659.
[3] Journal of Pathology and Bacteriology, 1904, vol. ix. p. 272.
[4] Ibid., 1903, vol. ix. p. 158.
[5] The American Journal of the Medical Sciences, 1894, vol. cvii. p. 31.

the child rapidly improved, and was able to run about and play. Although she had relief from pain and swelling, she did not appear to be well, and was languid. She was given quinine in tonic doses, and was not seen again until toward the end of September, when she began to exhibit choreic movements, which were particularly noticeable in her hands, feet, and face, and not unilateral; she also now complained of stiffness and soreness of the wrists. Three days later, September 29th, the movements had become so severe that the child could not swallow, and the sides of the bed had to be padded to prevent her injuring herself in her violent movements."

This condition continued until brought to the Infirmary on October 15th.

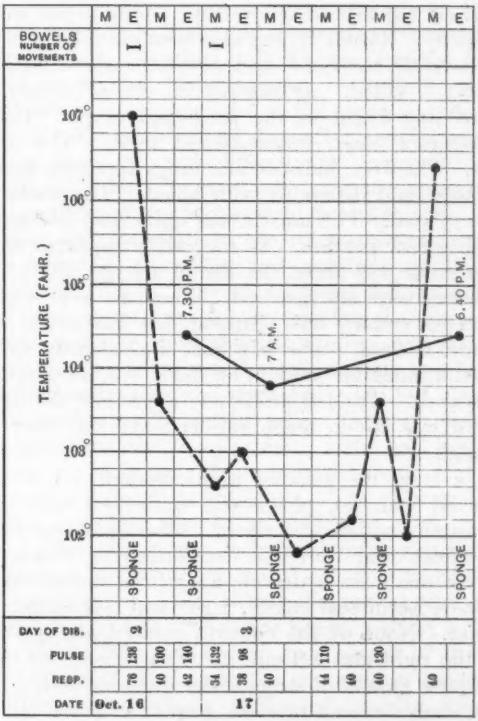
Upon admission, at 5 P.M., after a journey from Delaware, the child was perfectly limp and with but very slight choreic movements. She was unable to voluntarily move hand or foot, and the limbs hung as if paralyzed. She could not speak, and scarcely even swallow. The temperature was not taken, but the child seemed entirely apyretic. No heart murmurs could be detected. Pulse and respiration were both very rapid, and the latter shallow. On the morning of the 16th her temperature suddenly rose to 107°, and the choreic movements were excessive and so violent as to necessitate the padding of the sides of the crib. Her respirations were 76 per minute, and her pulse was 138.

Under sponging and chloral by mouth and rectum the temperature rapidly fell, becoming 101° F. by the morning of the 17th; the movements still, however, remained severe. Arsenic was first administered by the mouth and later hypodermically. No cardiac murmurs could be heard on the 16th, although they were carefully sought for, but on the morning of the 17th a soft apex systolic murmur was detected, which rapidly increased in intensity until her death, on the evening of the 17th, with a second rise of temperature to 106.5°. A blood culture was made on the afternoon of the day of her death. Although the greatest care was taken, the constant agitation was beginning to cause abrasions of elbows, shoulder-blades, hips, and heels. No examination of the urine was made, as none could be collected without catheterization, owing to the violent movements. No autopsy was allowed.

The accompanying chart shows the course of the fever.

Cultures were made from the median basilic vein about twelve hours before death. Three c.c. of blood were drawn with aseptic precautions and put into two flasks, one containing about 250 c.c. of litmus milk and the other about 250 c.c. of bouillon, to which 10 c.c. of hydrocele fluid had previously been added. After forty-eight hours the milk flask showed a marked acid reaction. The bouillon flask did not show any growths. Cover-slips from the milk flask revealed a small delicate diplococcus which occasionally formed chains of short length. The organism was immediately plated.

In agar plates both surface and deep colonies were exactly like those of streptococcus pyogenes. The morphology of the organism was that of a delicate diplococcus growing often in long chains in fluid media. Gram's stain was held, provided the decolorization in alcohol did not last more than two to three minutes. On plain agar slants the growth was exceedingly delicate and sparse. Separate tiny gray pinpoint colonies were scattered over the surface. On hydrocele agar the growth was somewhat more luxuriant, while



the condensation water showed marked clouding. On plain agar the cultures died within a week or ten days, but on hydrocele agar slants they could readily be kept alive for two to three weeks. This medium was, therefore, used entirely for the transplantation of the stock cultures. Milk was rapidly acidified and often clotted after a week's growth. In bouillon there was a scant growth collected in minute granules at the bottom of the tube. If, however, the reaction was alkaline (—10 Eyre) the growth was heavier. A growth could always be obtained in gelatin. There was no liquefaction.

On October 22d, five days after the organism had been isolated, two rabbits were inoculated intravenously with suspensions made with bouillon from a twenty-four-hours' growth on two hydrocele agar slants. Rabbit I. received 2 c.c. Rabbit II. received 1 c.c. On October 25th, three days after inoculation, both rabbits seemed well.

26th. Rabbit I. lies quite still and seems sick. When disturbed it moves about with difficulty and appears to drag right hind leg.

November 11th. Rabbit I. has remained definitely lame in left hind leg. Left ankle-joint is swollen. Hops about with a good deal of difficulty. Rabbit II. has also been quite lame in hind legs, but has apparently recovered, and now hops about with moderate ease. Rabbit I. killed. At autopsy 30 c.c. of cloudy port-wine colored fluid was found in the peritoneal cavity. Both pleural cavities contained clear, straw-colored fluid. The spleen was rather large. The liver, kidneys, and lungs appeared normal. The heart was large and distended with blood. The walls were thin and cavities dilated. The muscle was quite soft, friable, pale, and mottled with yellow patches. All the valves appeared normal.

The right ankle was about the size of a large cherry. The surrounding tissues were not involved. When the joint was opened a thick pultaceous creamy fluid escaped, but was mixed with some cloudy glutinous fluid. The left knee was slightly swollen, and when incised a moderate amount of thick, semitranslucent, glutinous fluid escaped. The left ankle was much like the right, except that the joint was not so much swollen. All the other joints appeared normal.

Cover-slips from the affected joints showed a few leukocytes, stringy mucoid material, phagocytic epithelioid cells, and many diplococci usually within leukocytes. The diplococci stained well in gentian violet, and were not decolorized by Gram's method. Cultures were made on hydrocele agar from heart's blood, liver, spleen, kidney, peritoneal cavity, right and left ankle, and right and left knee. None of the cultures showed any growth except those from the right and left ankles. From these two situations a meagre but pure growth of streptococci was obtained. The organism on subcultures agreed in every respect with the streptococcus previously described.

A third rabbit was inoculated with the organism obtained from the right ankle of Rabbit I. Three c.c. of a suspension of twenty-four-hours' hydrocele agar culture in bouillon were injected into the ear vein. For three or four days the animal appeared perfectly well. After this time he gradually became lame in the hind legs, and eight days after inoculation the left knee appeared definitely swollen. This was followed by involvement of the right ankle, and later by slight swelling of the joints of the forelegs. The animal rapidly grew much worse, and finally died eleven days after inocula-

tion. At autopsy extensive friable vegetations were found upon the mitral valve; there was an enlargement of the spleen, with anæmic infarctions of both that organ and the kidneys. Both ankles were greatly swollen and contained pultaceous material and sticky, glutinous fluid. There was a varying amount of involvement of the right knee and hip, left knee, right wrist, elbow, and shoulder, left shoulder and left wrist. A delicate diplococcus was found in cover-slips from the mitral vegetations in enormous numbers, and from the heart's blood and all the affected joints. The organism was grown from the heart's blood, mitral vegetations, spleen, liver, kidney, right ankle, knee, wrist and elbow, and left wrist. It proved to be a streptococcus identical with the one obtained from Rabbit I. and from the original blood culture.

A fourth rabbit was inoculated in the same way as the others, with 2 c.cm. of culture. About six days after inoculation the primary symptoms of lameness and difficulty in movements developed. Although the rabbit rapidly grew very lame and appeared quite ill, no definite swelling of the joints could be made out. The animal died nine days after inoculation. At autopsy practically every joint in the body showed some swelling and contained a moderate amount of thick, glutinous fluid. None of the joints were greatly increased in size, but some showed much more swelling than others.

Cover-slips from the right and left ankles, right shoulder, right and left elbow, and left wrist showed varying numbers of polymorphonuclear leukocytes and epithelial cells, but always quantities of diplococci, usually within cells. Cultures were made on hydrocele agar from the heart's blood, right and left ankle, and left wrist, and on plain agar slants from the liver. Colonies developed only on the tubes from the joints. The cultures from heart's blood, spleen, and liver showed no growth.

Finally, a fifth rabbit was inoculated intravenously in exactly the same manner as the others, with 1 c.c. of a twenty-four hours' hydrocele agar culture. The rabbit did not appear definitely ill for nine days, but by this time it was hopping about with difficulty, seemed ill, and preferred to crouch in a corner of the cage. On December 12th the animal appeared generally in better condition, but was still lame, and definite swelling of the left ankle-joint could be made out. After twenty-five days both ankles had become swollen, though the animal seemed generally better. The animal was killed on the twenty-fifth day after inoculation.

The peritoneal, pleural, and pericardial cavities were normal. The heart, spleen, liver, and kidneys did not show any marked pathological change. On the right ankle the Achilles bursa was found to be swollen to about the size of a cherry, while there was slight increase in the size of the ankle itself. The left ankle was very extensively swollen. All the joints were normal except the right wrist. Although this joint itself was not swollen, over one of

the extensor tendons there was a firm, rounded nodule about the size of a grape seed. On section a minute central soft point was seen. Cover-slips from this soft material showed a few leukocytes and epithelial cells, while here and there diplococci were occasionally found.

The organism was only recovered from the right ankle-joint.

A microscopic study of the organs from the four rabbits revealed the following conditions:

The heart muscle showed moderate grades of fatty degeneration, with swelling and parenchymatous degeneration of muscle fibres. In Rabbit III., which died of acute endocarditis, there were accumulations of small round cells and areas of polymorphonuclear leukocytic infiltration.

In one case there were areas of focal necroses in the liver. In the spleen and kidney of Rabbit III. definite anæmic infarctions were seen, while in the latter organ many of the small vessels and glomerular capillaries were plugged with masses of diplococci.

The synovial membrane from the joints, showing various degrees of involvement, presented marked pathological alterations.

In the earlier stages there was extreme œdema, congestion, and slight infiltration of polymorphonuclear leukocytes and small round cells. In the latter stages the cellular infiltration was more intense, and the fixed connective cells showed active proliferation. Epithelioid cells and small round cells were very numerous. The surface of the membrane was covered with polymorphonuclear leukocytes and granular débris. In one section many of the vessels of the synovial membrane were completely occluded by thrombi composed of fibrin, red blood corpuscles, and leukocytes.

Great numbers of diplococci could readily be demonstrated in sections stained by the Weigert-Gram method.

To sum up, we have a streptococcus isolated before death from the blood of a case of chorea, endocarditis, and rheumatism. This streptococcus is moderately virulent for rabbits when injected intravenously, and gives rise with the greatest constancy to a multiple arthritis which is rarely fatal, unless, as in one case, it is complicated by an acute vegetative endocarditis. The onset of the joint symptoms is only noticeable after a more or less definite incubation period of four to nine days. Before this time the animals appear perfectly well. The joint involvement usually starts with swelling and tenderness in the ankles. Probably there is pain, too, for the rabbits move but little and limp when made to hop about. The infection may remain localized or spread to practically all the joints in the body. Small swellings may also develop upon the muscle tendons. The streptococcus can be recovered with great regularity from all the affected joints.

The organism, from its morphological and biological properties, could not with any certainty be differentiated from the usual varieties of streptococcus pyogenes.

Walker has emphasized the fact that the "micrococcus rheumaticus" grows readily in filtered cultures of streptococci from sources other than rheumatic fever. Marmorek believes that by this procedure various closely allied species of bacteria may be separated.

We found that the particular streptococcus under observation grew fairly well in filtered twenty-four-hours' bouillon cultures of streptococci from several sources, but occasionally it happened that streptococci from the blood of puerperal septicæmia or other sources gave the same result. This particular biological test was, therefore, thought unreliable. The interesting fact was pointed out by Walker[1] that the micrococcus rheumaticus when grown in alkaline bouillon is capable of producing large quantities of formic acid, whereas other streptococci form very small amounts of this acid. In this connection the same author has found that formic acid is present in the urine of patients suffering from rheumatic fever. When our organism was grown in bouillon (—10 Eyre) for six to eight days, and subsequently distilled with sulphuric acid, formic acid could be demonstrated in the distillate.

But in spite of these minor variations the fundamental resemblance culturally is very close between streptococci isolated from the blood or lesions of rheumatic fever patients and streptococci from other sources. On the other hand, the results of animal experiments seem to bring out possible differences.

The streptococci that have so far been described in rheumatic fever show a remarkably constant and uniform predilection for the joints, heart valves, and serous membranes of the animals into which they are injected. Wassermann[2] produced joint lesions in eighty consecutive rabbits. Meyer[3] has found fungating and vegetative endocarditis in a surprisingly large number of animals after intravenous inoculation of streptococci obtained from the throat in rheumatic angina, while Poynton and Paine,[4] as well as Walker,[5] have observed monoarthritis and polyarthritis, endocarditis, pericarditis, and pleurisy in their animals. In our own cases the mode of onset, the joint lesions themselves, and the endocarditis were most striking. In every instance the lesions show such little variation and are so constant that they must attract attention. It is also worthy of note that, though the organism be passed through several animals, the virulence is little altered.

Experiments regarding the pathogenicity for animals of streptococci from sources other than rheumatic fever are not very numerous. This portion of the question we were, unfortunately, unable to investigate owing to the difficulty in securing the large number of rabbits which would be necessary for such work. Meyer found that with attenuated cultures of certain streptococci

[1] Loc. cit. [2] Loc. cit. [3] Loc. cit.
[4] Loc. cit. [5] Loc. cit.

joint lesions could be produced in animals. This result was, however, not constant. With small doses the joints became swollen, and later went on to suppuration, the condition finally ending in death. With large doses a septicæmia, sometimes attended with joint symptoms, was observed. Glaser[1] has also observed multiple arthritis in rabbits following intravenous injections of various strains of streptococci. Under ordinary circumstances intravenous inoculations of the lower animals with virulent streptococci give rise to a rapidly fatal septicæmia, but if cultures of attenuated cocci are injected either a monoarthritis or polyarthritis may follow. The latter result is variable.

A spontaneous endocarditis following intravenous inoculations of streptococci is perhaps even rarer than arthritis. Weichselbaum,[2] in a series of experiments, found it necessary to injure the heart valves before vegetations could be obtained, and although Pasquale[3] was able to produce subcutaneous abscesses, general septicæmia, hemorrhagic infarctions of the lung, phlegmonous œdema, and hydropericardium in thirty-eight rabbits after subcutaneous and intravenous injections of streptococci from many different sources, he does not mention the occurrence of either arthritis or endocarditis. Widal and Bezancon[4] obtained a streptococcus from the mouth which gave rise to acute endocarditis in a rabbit after subcutaneous inoculations. In ninety-five experiments made with other streptococci this result was not again met with.

One noticeable feature of all these observations is the variation which many of these organisms show in their virulence for men and animals. Streptococci which produce fatal septicæmia in human beings may show very slight virulence for animals, while organisms grown from local abscesses may be rapidly fatal for animals.

In view of the fact that streptococci isolated from sources other than the blood or complicating lesions from cases of rheumatic fever do, under certain circumstances, produce arthritis and endocarditis in animals when injected intravenously, it is surprising that the English observers, particularly, have made so few experiments to control their work. This side of the question needs to be thoroughly investigated before definite conclusions can be drawn as to the specificity of the streptococcus described as the cause of rheumatic fever. Indeed, several observers, among others Menzer,[5] believe that rheumatic fever is caused not by a specific coccus, but by many varieties of streptococcus.

Most observers are agreed that it is impossible to obtain a growth of bacteria either from the blood or joint fluids of cases of rheumatic

[1] Verhandl. des XIX. Cong. f. inn. Med., 1901, p. 471.
[2] Ziegler's Beiträge, 1889, Bd. iv.
[3] Ibid., 1893, Bd. xii. p. 433.
[4] Le semaine méd., 1894, p. 195.
[5] Loc. cit.

fever which recover. Phillip[1] has recently reported such a series of negative results, and in the cases of rheumatic fever reported from the Johns Hopkins Hospital by McCrae[2] cultures from the blood and joint fluids never gave a growth of streptococci. Except in the fatal case reported we have had the same experience at the Pennsylvania Hospital. One must not overlook, therefore, the possibility of a streptococcus infection supervening as a terminal event in the fatal cases of rheumatic fever. Under these circumstances the condition might be similar to that which one finds in scarlet fever and variola.

SUMMARY. In a fatal case of rheumatism, endocarditis, and chorea a streptococcus was isolated from the blood before death. This organism did not differ materially from the common varieties of streptococcus pyogenes in cultural properties, but produced very characteristic lesions in rabbits when injected intravenously. Such inoculations were always followed after a few days' incubation period by a multiple arthritis which usually started in the ankles. In one rabbit extensive vegetations were found on the mitral valve, while typical infarctions were seen in the spleen and kidney.

We believe that this streptococcus is the same as that described by Wassermann, Meyer, Poynton and Paine, and Walker, and considered at least by the last three observers to be the specific cause of rheumatic fever.

OPERATIONS FOR PRIMARY CARCINOMA OF THE LIVER.

REPORT OF A CASE WITH FREEDOM FROM RECURRENCE AT END OF SIXTEEN MONTHS.[3]

BY LEONARD FREEMAN, M.D.,
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PRIMARY carcinoma of the liver is a rare affection, Hansemann finding it but six times among 258 hepatic tumors reported from the Berlin Pathological Institute from 1880 to 1889; while Eggel computes, from various sources, that it occurs about once in every 2000 autopsies. In 800 operations upon the liver, Kehr encountered but one operable cancer.

It is either nodular or diffuse (carcinomatous cirrhosis), the former variety being much more common than the latter. The

[1] Deutsch. Arch. f. klin. Med., 1903, Bd. lxxvi. p. 150.
[2] American Medicine, August 8, 1903.
[3] Read before the American Surgical Association, St. Louis, June 16, 1904.

nodules may be single or multiple, large or small. According to most observers, primary carcinoma is more apt to exist as a single nodule, although there is difference of opinion on this point.

The single primary nodule is alone amenable to surgical treatment. It may occur in any portion of the liver, but is usually found near the inferior border of the right lobe. It is generally met with during the "cancer age," but may be seen in younger individuals, a number of cases having been reported in patients under twenty years. It may arise from the endothelial lining of the bile-ducts or from the hepatic cells themselves, the latter origin being demonstrated by the secretion of bile in metastatic nodules. Metastases are common. There is almost always more or less coexisting cirrhosis of the liver. Whether the cancer arises from the cirrhosis or the cirrhosis from the cancer is still a disputed question.

There is a very close relation between tubular adenomata and primary carcinomata. They often co-exist in the same tumor; and where a number of nodules are present, some may be adenomata and others carcinomata, while others are in a stage of transition. Some writers, such as Terrier and Auvray, class the adenomata as adenocarcinomata, their malignancy being indicated by the metastases which frequently take place.

The only hope for permanent cure of primary carcinoma lies in early operation; but the diagnosis at this time is extremely difficult, owing to the small size of the tumor and the frequent insignificance or even total absence of symptoms. Generally, when the tumor is large enough to be felt from without, or when icterus or ascites has appeared, it is too late for an operation to be of service, except for purposes of palliation.

Statistics are difficult to obtain, especially with the limited literature at the writer's command. In 1901 Terrier and Auvray collected 52 operations for hepatic tumors. Of these 9 were primary carcinomata and 1 secondary. Ten of the 52 cases died, $19\frac{2}{3}$ per cent. Local or general recurrence has been the rule, but there are some exceptions which afford encouragement for further efforts. For instance, one case (Schrader) was well at the end of seven years, and another (Terrier) at the end of five months. A favorable case reported by Lücke, in 1890, however, was probably a gumma (Kehr) and should not be considered in this connection.

Methods of Operating. There are two principal methods of operating, both of which have numerous advocates: one in which the stump of the liver is sunk in the peritoneal cavity, and the other in which it is fastened in the wound, thus rendering it extraperitoneal, as was formerly done in hysterectomy. Owing to recent improvements in technique, the former procedure is as free from danger of hemorrhage as the latter, and is certainly preferable from the standpoint of asepsis and rapid and satisfactory

convalescence. In addition, there are cases in which the liver cannot be mobilized sufficiently to permit of secure extraperitoneal fixation, even by attaching it to the peritoneum alone—the "funnel method" of Riedel.

In case the extraperitoneal method is adopted, however, there are three ways of proceeding:

1. The operation may be done in two stages. In the first, the portion of liver containing the tumor is sutured into the abdominal wound, where it is permitted to remain until firm adhesions occur; and in the second the tumor is removed. This suggestion of Tillmanns, it may be remarked, has not been generally adopted.

2. The liver may be fastened in the wound by sutures, or possibly by needles passed through its substance, and surrounded by an elastic ligature, which remains until gangrene appears, when the dead part, including the tumor, is cut away (Lücke, Terrillon). It would seem, however, that the danger of sepsis during this time must be considerable, to say nothing of other objectionable features.

3. After securing the liver in the incision, the tumor may be excised at once.

Incision. No special form is indicated. It can be vertical or transverse, along the costal margin, or curved according to Bevan; but it should be so situated as to expose the tumor to the best advantage and afford plenty of room. It may occasionally be necessary to resect the cartilages of the eighth to the eleventh ribs (Lannelongue), or even to turn up a flap from the chest wall (Micheli), or mobilize the liver by dividing the ligaments which suspend it (Langenbuch).

Hæmostasis. After exposing the tumor the remainder of the operation consists practically in the control of hemorrhage, the actual excision of the growth usually presenting no serious difficulties. The fear of uncontrollable bleeding has greatly retarded the advancement of hepatic surgery, and it is only within the last few years that methods have been devised which have inspired a reasonable amount of confidence.

Experience has shown that no matter what precautions have been adopted, it is wise to reinforce them with ample gauze packing, especially when the cut surface of the liver is replaced within the abdomen. Failure to do this has led to disaster from delayed hemorrhage.

Numerous suggestions have been made regarding the control of bleeding during the operation and subsequently. No one of them is entirely satisfactory, but several are sufficiently so to justify their use. The principal methods are as follows:

(*a*) *Temporary Hæmostasis.* 1. Constriction of an entire lobe of the liver by an elastic ligature. This is particularly applicable to a movable left lobe, although Israel has succeeded in applying

it in a single instance to the right lobe during the removal of a sarcoma in a child.

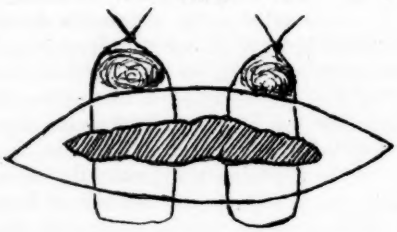
2. Digital compression furnished by assistants. This can be resorted to in favorable cases only—where the tumor is pedunculated or fairly well isolated near the border of the liver.

3. Provisional ligature of the vessels in the hepaticoduodenal ligament. This was suggested by Langenbuch, but I am not aware that it has been employed by others.

4. Parenchymatous injections of adrenalin chloride (Gualdrini). If this has any appreciable effect, it can be upon the smallest vessels only, and therefore its value seems questionable.

(*b*) *Permanent Hæmostasis.* 1. The liver may be sutured into an incision parallel to the costal margin in such a manner that the edges of the wound exert sufficient pressure to check bleeding (Chapot-Prevost). This is perhaps best accomplished by means of several mattress sutures passing through the tissues at the border of the ribs, deeply through the liver, and out through the abdominal wall below. They are then returned in reverse order and tied over compresses at their points of insertion (Fig. 1).

FIG. 1.



2. Sutures of heavy silk may be inserted through the abdominal parietes, passed under the bleeding points in the liver, brought out again, and tied on the surface of the skin (Ullmann).

3. The actual cautery. This has often proved unreliable and should not be trusted to alone, although it may be valuable in checking mere oozing.

4. Cauterization with steam at 70° C. (Caponago), or heated air (Abramowitsch). Although both these methods have been highly spoken of, they are probably no more effective than the actual cautery and not nearly so convenient. They are not frequently employed.

5. Compression by gauze is very valuable as an adjunct to other procedures, and should always be resorted to. In order to hold the gauze securely in place it may be advisable to fasten it with sutures (Hochenegg), or even to sew it between the edges of an incision.

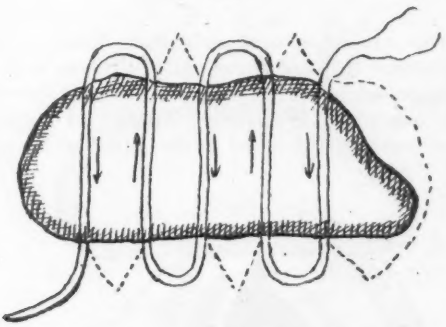
6. Immediate suture of an incised wound is ideal, but seldom practicable.

7. In order to prevent ligatures from tearing through the friable substance of the liver, an accident much feared before the experiments of Kurznezow and Pensky, Delbet strung upon filaments of catgut a number of hollow sections of decalcified rabbit bones, while Segale recommended tubes of ivory or ebony, and Cecherelli and Bionchi plates of whalebone. These ingenious devices are, however, inferior to others which are less complicated and troublesome.

8. The use of permanent forceps or clamps is often of great service.

9. The elastic ligature, especially in pedunculated tumors, has had many adherents. It is generally used extraperitoneally, although not necessarily so. If the pedicle is large the ligature

FIG. 2.



The continuous lines represent a continuous double thread passed backward and forward through the liver by means of a blunt needle, so as to form a series of loops. By dividing the loops, separate ligatures are obtained, which are tied as indicated by the dotted lines. (Terrier and Auvray.)

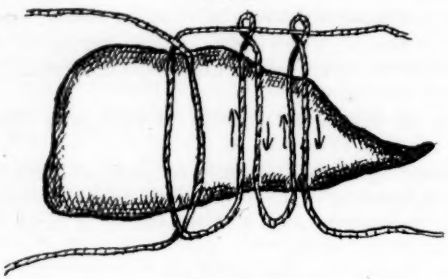
may require tightening from time to time (Lücke), and care must be used to prevent too rapid cutting of the tissues.

10. It has been suggested that bleeding may be checked by stitching omentum over the raw surface. Although this may occasionally be of some service, it can have no extended applicability on account of its unreliability and the amount of time consumed.

11. A method which has attracted much attention was presented by Kurznezow and Pensky in 1886 (Fig. 2), and modified by Auvray in 1897 (Fig. 3). It depends upon the principle that when a ligature is tied tightly about a section of liver, not too large, the parenchyma gives way, but the contained vessels are gathered

into a bundle and held firmly (Fig. 4). The procedure is certainly effective when properly carried out; but it requires time and care, and the somewhat elaborate technique is usually forgotten when needed, which is apt to be unexpectedly.

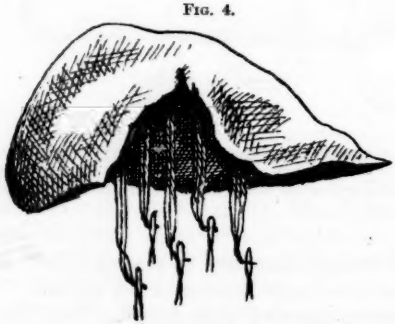
FIG. 3.



Terrier and Auvray.

12. The liver substance surrounding the tumor may be easily ligated with narrow strips of gauze pulled through with long, blunt forceps, as suggested by W. Müller, who treated the stump, however, extraperitoneally. The writer's method of employing these strips intraperitoneally is detailed in the report of his case.

FIG. 4.



Terrier and Auvray.

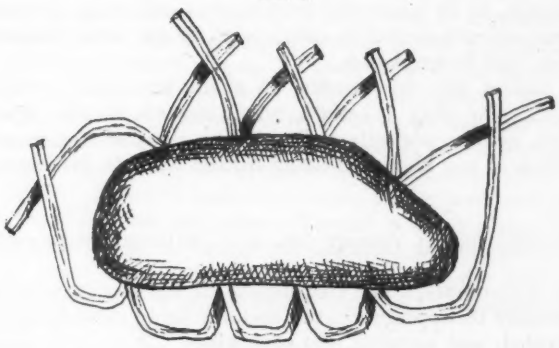
13. In some instances, either alone or in connection with other procedures, the hepatic vessels may be seized with forceps, pulled out from the cut surface, and easily ligated. Experiments have shown that they will stand a traction equal to 750 or even 850 gr.

REPORT OF CASE. A well-developed, muscular, locomotive engineer, aged twenty-seven years, had been annoyed for a year

or more by heaviness and moderate pain in the region of the gall-bladder, with occasional exacerbations accompanied by slight jaundice and marked indigestion. Examination revealed a hard, irregular tumor, apparently about the size of a walnut, although the patient stated that it sometimes became larger and more tender. It occupied the position of the gall-bladder and moved up and down with respiration. A diagnosis was made of a gall-bladder tightly filled with stones, although this was done with reservation, because of the mildness of the symptoms in spite of the size, irregularity, and hardness of the tumor.

Operation (*January* 20, 1903). A longitudinal incision through the right rectus revealed a hard, nodular tumor of the left lobe of the liver, just to the left of the notch. It was the size of a large fist, buried almost completely in the substance of the organ, and without

FIG. 5.



a pedicle. The greater part of the growth lay beneath the free hepatic border, so that a small portion only could be felt by abdominal palpation. There were extensive omental adhesions, but no enlarged glands, and the remainder of the liver was free from involvement as far as could be detected. The gall-bladder was normal.

After enlarging the incision it was decided to isolate the tumor by means of ligatures formed from narrow, folded strips of gauze, such as are found in every operating-room. The liver was perforated with long, blunt forceps and the strips pulled through—at first two strips, and then, through each successive hole, an end of the previous strip together with a fresh one. A series of loops were thus obtained, each one enclosing a considerable amount of tissue (Fig. 5). These were slowly and forcibly tightened and tied, thus effectually compressing the liver, but not cutting it as do

ordinary sutures. Hemorrhage from the perforations was prevented by the presence of the gauze.

The tumor was then removed by cutting through normal liver tissue with a scalpel, no bleeding following the section except from a single vessel not included in the ligatures. After sinking the stump in the abdomen it was packed around with gauze, the ends of which, together with the ends of the strips, being brought out through the partially open wound.

The progress of the case was uneventful except in one respect—the removal of the gauze ligatures. The knots being buried deeply in the wound, they could not be untied or even cut with certainty. After some difficulty several strips were finally extracted; but the others resisted all efforts until bands of rubber were attached to them so as to exert constant traction, when they came out promptly and easily and without pain. At another time I should be inclined not to tie the strips, but merely draw them tight and clamp them with forceps, or tie them with catgut, thus admitting of comparatively easy extraction; but in case a strip should stick, elastic traction could still be employed.

The patient left the hospital in about six weeks, completely recovered. On May 18, 1904, about sixteen months after the operation, he was perfectly well, with no signs of recurrence, no disturbance of any kind, and doing regular work on his engine.

PATHOLOGICAL REPORT (DR. J. A. WILDER, OF DENVER).

Gross Appearance. The free surface of the specimen is irregularly nodular in appearance, the nodules being smooth, rounded, and elevated, and merging into each other.

On section the tissue which forms the greater part of the specimen cuts with considerable resistance, being very tough and fibrous, and light in color, in marked contrast to the liver tissue proper. In several places a sharp line of demarcation can be seen between the neoplasm and the liver substance.

Microscopic Examination. Specimens hardened in formalin and alcohol, embedded in celloidin, and stained with the usual stains. Sections were made from blocks taken from the periphery of the neoplasm and from its central part, as well as from blocks including both liver tissue and neoplasm. Sections from the peripheral portion consist of a well-marked stroma of dense connective tissue which forms irregular alveoli in which the cellular material, which is of the glandular epithelial type, is compactly arranged. In some places the cells are so arranged as to give the appearance of atypical and irregular gland tubules, the cells approaching the columnar type and being arranged in several layers. No basement

membrane can be seen. In most fields the alveolar arrangement with the cells completely filling the spaces is most conspicuous. In some places the cells are arranged in long columns which are surrounded by the connective tissue. The cells are large and have large round or spheroidal nuclei that take the stain with moderate intensity and contain distinct nucleoli. The cytoplasm is present in considerable amount, its periphery in some of the cells being distinctly outlined, but in the majority indistinctly, the cell bodies appearing to have coalesced.

The majority of the cells that can be accurately measured are from 16 microns to 22 microns in diameter, their nuclei measuring from 7 to 12 microns. Sections from the blocks in which both liver tissue and neoplasm were included show a broad band of connective tissue between the two, which has been infiltrated in various places by the tumor cells. The liver cells differ very materially from those of the neoplasm in general appearance, staining reaction, arrangement, and regularity. They show a moderate amount of parenchymatous degeneration. The stroma is abundant and consists chiefly of adult fibres of connective tissue, giving the picture of scirrhus in many places. In some parts the stroma is infiltrated by collections of lymphoid cells. The vascular supply is rather poor, but a few vessels with well-developed walls are present in the connective tissue. The stroma contains also a few apparently normal bile-ducts. An effort at encapsulation by dense connective tissue appears to have been made at the periphery of the nodules, but this tissue had been infiltrated in many places by the epithelial cells. The distinctly adenomatous appearance of the growth in some places and the characteristics of the epithelium present are suggestive of the possible origin of the neoplasm from the bile-ducts.

Histological Diagnosis. Adenocarcinoma.

THE SHAPE OF THE CHEST IN HEALTH AND IN PULMONARY TUBERCULOSIS.

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and

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Introduction. Since the time of Hippocrates the shape of the human chest and its changes in disease have been often discussed. On account of the widespread prevalence of pulmonary tubercu-

losis the attention of many observers in all ages has been drawn to the disease, and much has been written about the shape of the chest in pulmonary tuberculosis. Hippocrates described a type of chest in pulmonary tuberculosis which is smaller than the normal chest, but has the same general outline. The scapulæ do not lie flat on the posterior wall, and this projection has given the name alar to this type of chest. Galen has added that the chest is narrow and shallow, and Gee[1] states that the anteroposterior diameter is especially small, "but the diminution in capacity presented by the alar chest does not necessitate any great change in the outline which a horizontal plane of the thorax naturally presents." Dr. Gee then describes a second form of chest frequently occurring in pulmonary tuberculosis, the flat chest, which has its anteroposterior diameter lessened. These views have been generally accepted (Osler,[2] Musser,[3] Fraenkel,[4] Steel,[5] etc.) without further investigation, and where any authority is mentioned reference is generally made to Gee.

In 1897 Dr. Woods Hutchinson called in question these generally accepted views and stated that the flat chest of phthisis was only apparent, not real. A series of measurements was instituted at the Adirondack Cottage Sanitarium in 1901, with a view to throwing additional light on the question. It was thought too that any physical characteristic should be reduced to a basis of measurements, and entire reliance should not be placed on the judgment of the eye.

HUTCHINSON'S THEORY. In the *Journal of the American Medical Association*, September 11, 1897, Dr. Hutchinson first published the result of his chest measurements. He further elaborated his views in his book (*Studies in Human and Comparative Pathology*), and again in 1903 (May 2) wrote in the *Journal of the American Medical Association* an article, "Is the Consumptive Chest Flat?" He compares all chests by means of the "chest index," which is defined as the ratio of the anteroposterior diameter to the transverse diameter. He takes for his normal type the results obtained from the Yale anthropometric table compiled from the measures of 2300 students by Dr. Jay W. Seaver and 50 measurements made by himself on soldiers at Fort Porter. His tuberculous type is based on measures from 350 cases, mainly from various hospitals (Brompton, etc.) and in advanced stages of the disease, collected by various medical men as well as by himself.

He concludes from these measures that:

"1. The typical tuberculous chest is round instead of flat and has an average index of about 80, nearly ten degrees above the normal (70).

"2. This type of chest precedes the disease.

"3. It is an abnormal persistence of the fetal, infantile, and child type of chest.

"4. Any chest more than eighteen years of age that shows an index of 80 or higher should be regarded as abnormal and as rendering its possessor more than usually liable to tuberculosis.

"5. The occurrence of such a chest in any person over eighteen years of age suspected of tuberculosis raises a strong probability of the disease.

"6. The chests of growing boys and girls should be systematically measured at stated intervals, and whenever the index is found distinctly higher than the normal for their age active measures should be taken to remedy the defect.

"7. All those sports and exercises which involve wide-swinging use and play of the arm, chest, shoulder group of muscles, such as tree climbing, swinging from ladders, from rings, from bars, ball throwing, spear hurling, tennis, swimming, will tend to correct this defect and flatten the chest down to its proper index."

THE INDEX OF THE NORMAL CHEST. In order to discuss any variation, it is of the utmost importance to settle definitely if possible upon a normal. Almost at the beginning of this inquiry it was felt that before conclusions could be safely drawn it was necessary to have further data in regard to the normal adult chest. Information as to the absolute measures at various ages, the effect of age and development on the index after childhood, the range of index in normal individuals, etc., were of fundamental importance. That the average index of the soldiers who were older men and under special physical training was higher than that of the Yale students seemed worthy of attention. A comparison of chest measures in patients emaciated from causes other than pulmonary disease seemed also desirable. The question of the female chest, which Dr. Hutchinson thought had normally a higher index than the male, had also to be investigated. After searching in various directions with very little result, Dr. D. A. Sargent, of the Hemenway Gymnasium, at Harvard, kindly offered to take a series of measurements, and later forwarded the measures of 540 males and 180 females. An anthropometric table, compiled by Annie L. Barr, Director of the Women's Gymnasium, University of Nebraska, was also obtained. Certain measurements quoted by Musser and Gee, notably those of Otis, of Boston, have been used. Dr. Stroud, of Tufts College, has been so kind as to send measurements of 102 of his college students. The anthropometric table of 2300 Yale students, compiled by Dr. Seaver, has also been used in estimating the normal.

The Yale table, from which Dr. Hutchinson draws his normal, differs markedly from the other sources of information. The 50 soldiers which he measured at Fort Porter give an index of 73.9, and two other short series (where numbers are not stated) give 71.5 and 72.6, respectively. While the individual measures for the Yale cases are not obtainable, yet it is highly probable that the average index would not differ materially from the index obtained by using

the normal diameters (69.3). The measures of 540 Harvard students (males) indicate an average index of 77.5. In a series of measures taken by Dr. E. O. Otis, 1250 of the depth of the chest and 400 of the breadth of the chest, the index resulting from the averages was 75.8, agreeing very closely with Dr. Sargent's. Several measurements given by Gee would indicate a normal index of 74 or 75. Dr. Stroud's measures taken at Tufts College have an average index of 68.2.

Taking the series of fetal, infantile, and child indices as given by Dr. Hutchinson, it is found that the change during the first few years is large, but rapidly decreases as age advances. This fact has long been recognized. If a curve is plotted, it is found that, taking Dr. Sargent's or Dr. Otis' figures at the mean age (about twenty years), the indices of 77 and 76 form a consistent continuation, but the index from Dr. Seaver's Yale measurements cause a sharp bend in the curve. However, combining the Yale, Harvard, Otis, and Fort Porter measures, a normal index of 73.2 is obtained.

The index of the normal female chest is stated by Dr. Hutchinson to be higher than that of the male. The average index of the female student at the University of Nebraska from Miss Barr's measures is 67.7. From 180 female cases measured by Dr. Sargent, the average index was 70. From this it seems that the female chest index is lower than the male—*i. e.*, the female chest is flatter than the male.

Method of Taking Measurements. After the collection of these various data it was found that the measures were not all taken under exactly the same conditions, and that allowance would have to be made for this. Hutchinson's measurements were made at the level of the nipples or of the middle of the fourth intercostal space at the post-expiratory pause. Sargent's were made at the level of the nipples after a natural inspiration, and Seaver's at the same level "in ordinary quiet position without forced inspiration," while Otis recorded his presumably at the same level at repose and on inflation. To estimate what allowance should be made for the variations caused by these differences in obtaining the measurements, 25 cases at the Adirondack Cottage Sanitarium were measured. It is fully recognized that the respiratory movements in these cases may be slightly less than in the healthy, but still some guidance can be obtained from them. The average difference in the anteroposterior diameters taken after quiet inspiration and expiration was 0.42 cm., that of the transverse 0.52 cm., amounting in each case to about 2 per cent. of the absolute measures. It was early recognized that the level of the nipples varied considerably, and it was thought better to select some bony prominence as a guide. Hutchinson used, in some cases, the middle of the fourth interspace, but on account of confusion in estimating this point (Hutchinson did not state whether he took the level at the sternal border or in the nipple line), it was

thought better to select the level of the fourth costal cartilage. To determine what variations might occur from measurements taken at these different points, 25 cases at the Adirondack Cottage Sanitarium were measured. Measurements of the anteroposterior and transverse diameters were taken at the level of the juncture of the fourth costal cartilage and the sternum and at the level of the nipples. It was found that these two levels varied considerably, depending upon the obliquity of the costal cartilages and the ribs. The difference in level ranged from 1.5 to 5.5 cm., and averaged 3.4 cm. The transverse diameter varied very little, the average difference, an increase at the nipple level, being less than 1 per cent. (0.8 per cent.). The anteroposterior diameter, however, varied considerably over 3 per cent. (3.6 per cent.), being deeper at the nipple level. This change in relative measurements caused a change in the index of about 3 per cent., or two degrees—*i. e.*, from 69.4 at the level of the fourth costal cartilage to 71.4 at the level of the nipples. From these observations, especially from the difficulty in obtaining the transverse diameter at the level of the fourth costal cartilage, it is best to select the junction of the fifth costal cartilage with the sternum as the level on which to take the diameters of the chest. The post-expiratory pause seems to be the best time in which to take the measurements.

This experience brings into prominence the desirability of greater uniformity in the method of taking anthropometrical measures, so that the data collected by different observers may be compared or combined, and so that the collectors of any such measures in the future may know what is the best method of procedure.

Statistical Methods. In any investigation depending largely on the analysis and comparison of series of measurements, the choice of the statistical methods to be employed is of great importance. The use of the average or arithmetical mean to represent a series oftens leads to serious error, and is only appropriate under certain well-defined conditions:

1. The series must be homogeneous in regard to any characteristics which might affect the result. A familiar illustration of error arising from neglect of this condition is furnished by a comparison of the general death rates of two cities in which the age distribution of the population is very different. While the death rates for each age may be the same in both places, yet the general total death rates may vary widely, owing to the population of one city consisting mainly of those in the prime of life, while the other contains a much larger population of children and aged persons, among whom the mortality is much higher.

2. Variations from the normal must be, *a priori*, equally probable in either direction; in other words, the law of variation must be the binomial or exponental law. Many of the measurements of the human body do not fulfil this condition, as has been repeatedly

pointed out. Further evidence of this is furnished in the study of the chest measurements, which follow. Even when both the foregoing conditions are fulfilled, the average may not satisfactorily represent the tendency of the series, and is by itself of little value for making comparisons, as it in no way indicates the degree of divergence from the mean, which is in general one of the most important characteristics of a group of measurements.

Of the two most fruitful methods, one consists in arranging the measures forming the series in the order of their respective magnitudes, showing the number of cases at each magnitude or in the interval between a set of equidistant magnitudes. The magnitude or interval under which the greatest number of cases occurs is then taken as the normal. When the above results are plotted on squared paper, the magnitudes or intervals being the abscissæ, and the numbers of cases the ordinates, the resulting curve gives a graphic representation of the series in a very convenient and suggestive form. When a series is homogeneous and not subject to any influence rendering variation in one direction more probable than in the other, a symmetrical curve approximating to the type of the probability curve is obtained. Any variation from this type demands careful consideration. When a series is small and gives a very irregular curve, it is often advantageous to group several consecutive magnitudes together, and thus secure a more regular progression, taking care, however, that in so doing no essential characteristic of the series is lost. The other method referred to is that due to Galton, and is known as the percentile method. This consists in arranging all the measures in the order of their magnitude and taking the central value as the normal, arranging the other values in accordance with the percentage of the total cases which exceed or fall short of them.

The degree of confidence which obtained results should warrant is often hard to determine. In general the weight of an average is proportional to the square root of the number of measures of which it is the mean—*e. g.*, a series of 400 cases has only twice the value of a series of 100. When, however, several independent series give the same result, the reliance warranted is greater than that called for by the same total number of cases all belonging to one series. The average gives sometimes undue weight to a few abnormal cases and to errors, and the other two methods are far superior in this respect. The "frequency" method is generally preferable where it is desired to present the results of a series in a form giving the greatest amount of information in the smallest space. When the frequencies are given, the average and percentiles can easily be calculated; where only the average is given, even with a statement of the average deviation or error, neither the frequencies nor the percentiles can be gotten; and where the percentiles only are given the calculation of the average and the frequencies is not possible. The

graphical method of presenting the frequencies is, perhaps, the most satisfactory way of all. "When there is some degree of asymmetry," writes Prof. Venn, of Cambridge, "it is the maximum ordinate which would have to be considered as a mean to the exclusion of the others, for no appeal to an arithmetical average would guide us to this point, which, however, is to be regarded, if any can be so regarded, as marking out the position of the ultimate type."*

THE EFFECT OF AGE, GROWTH, AND DEVELOPMENT ON THE SHAPE OF THE CHEST. After growth in height has practically ceased, the development of the body in other ways still continues. The data for discussing this question are, however, very few. The Adirondack Cottage Sanitarium cases being underdeveloped and diseased, cannot be used as a certain guide, and the measurements of college men and women are very few beyond twenty-two years of age. The 50 measurements of soldiers collected by Dr. Hutchinson commence at twenty-one, and, to a certain extent, supply the want, though, as these men are constantly undergoing special training, too much weight cannot be given to inferences derived from them. However, taking all the series together, it seems safe to conclude that development in both diameters of the chest continues much longer than increase in total height.

The increases in the diameters from birth to manhood are, as stated before, not proportionate, the transverse increasing more rapidly than the anteroposterior diameter. This tendency of a decrease of index appears to continue up to a certain period (eighteen to twenty-four years), and then a change occurs, resulting in a tendency of an increase of the index. The definite cause of this increase of index has not been determined. Gee has noted that in advanced years there is some tendency for the chest to revert to the configuration of childhood. In every series of measurements available this tendency is shown. The Harvard measurements show the early decrease and later increase of the chest index with age (sixteen to eighteen years, index 78.3; nineteen years, 76.3; twenty years, 77.3; twenty-one years, 76.6; twenty-three years and over, 79.6). While in the tuberculous cases no doubt other factors may occur, still the tendency is very striking.

COMPARISONS OF VARIOUS SERIES OF MEASURES. The various series of measurements have been represented graphically and some shown in the accompanying diagrams, but each measurement is considered separately. It has been thought best to treat separately the measurements obtained in cases of pulmonary tuberculosis from those obtained in normal chests.

Table I. shows the average (absolute) changes in the various measures concurrent with age and development. The tuberculous cases follow the same law.

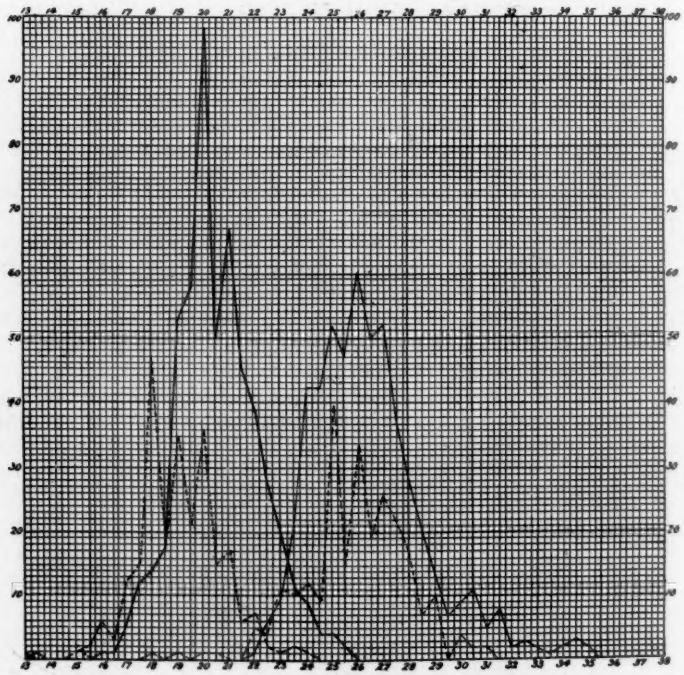
* Logic of Chance, p. 455.

TABLE I.—Variation of chest measurements for age and sex.

Sex.	Ages.	Cases.	Antero-posterior diameter.	Trans-verse diameter.	Index.	Length.
Male	16–17–18	131	20.16	25.77	78.3	33.14
"	19	113	20.40	26.77	76.3	32.96
"	20	104	20.87	26.75	77.3	33.25
"	21–22	117	20.60	26.67	76.6	33.21
"	23 & over	75	20.93	26.45	79.6	34.05
Female	16–17	34	17.45	24.72	70.6	29.98
"	18	73	17.57	24.95	68.0	30.51
"	19	49	17.81	24.66	72.2	31.47
"	20 & over	24	17.79	25.10	71.1	31.59

THE SHAPE OF THE CHEST IN HEALTH. *The Anteroposterior Diameter in Males.* The Fort Porter maximum is most marked at 20.5 cm.,* the Harvard at 20 cm.,† and the Tufts at 18 cm. (See Chart I.)

CHART I.



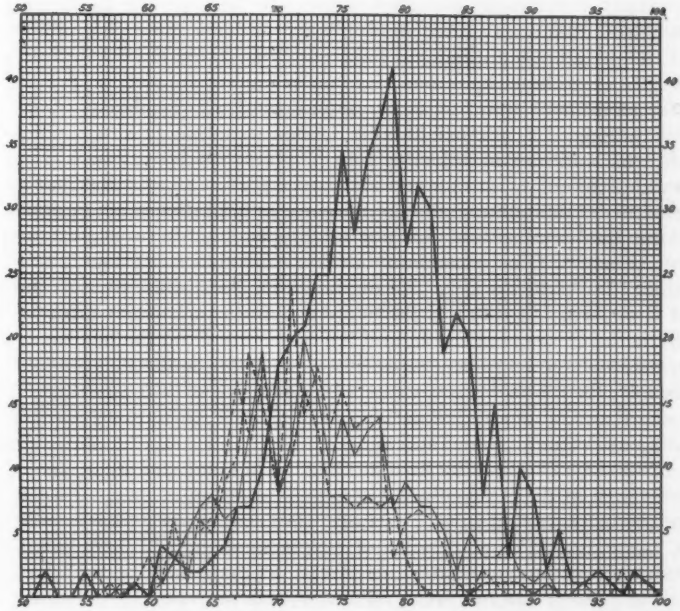
* The Fort Porter cases were measured by Dr. Woods Hutchinson.

† It should be recalled that the Harvard measures are taken at the post-inspiratory and not post-expiratory pause, causing a difference of about half a centimetre.

The Transverse Diameter in Males. The Tufts maximum is 28 cm.; the Harvard, 26 cm.; the Fort Porter, 26.5 cm.; and the Yale mean is 27 cm. The Fort Porter cases show a tendency toward a submaximum at 28.5 cm. In each series there is a less strongly marked normal transverse diameter than in the case of the normal anteroposterior diameter. This would in all probability indicate that there is in general a greater variation in the transverse diameter than in the anteroposterior. (See Chart I.)

Chest Index in Males. The variations in the frequency of the chest index average is striking: Harvard, 79; Fort Porter, 73; and Tufts, 66 and 69. (See Chart II.) The ratio of the means at Yale is 69.

CHART II.



The Length of the Chest in Males. The length of the chest has a comparatively wide range, between 33 and 36 cm., and no well-defined maximum.

The Anteroposterior and Transverse Diameter in the Female. For the anteroposterior diameter the Sargent measures have a maximum at 17 cm. For the transverse diameter the Sargent maximum is at 24.5 cm.

The Chest Index in the Female. The tendency of the chest index seems to be lower than in the case of males. (See Chart II.) The

Sargent cases have a maximum at 68. The ratio of the means of the University of Nebraska is 68.

Length of the Chest in Females. The Sargent data show that the range of length is about 3 cm. less than in the male.

THE SHAPE OF THE CHEST IN PULMONARY TUBERCULOSIS. Few measurements of the chest in pulmonary tuberculosis taken previous to this time have been found of value for this study, as they do not include the diameters. It is well always to bear in mind that individuals with apparently normally-shaped chests may be liable to pulmonary tuberculosis—*i. e.*, chest configuration renders no one immune. "My examination of some 6000 nude chests," says Alison,[6] "at the Consumption Hospital (Brompton) has established several facts in connection with this subject. The first is this: Comparatively few greatly distorted chests are seen among phthisical patients; I believe not more in proportion than are found in persons not suffering from phthisis. I have met the greatly distorted chest, the greatly gibbous back and sternum of rachitis in not more than some six persons suffering at the same time from decided phthisis; while among this number of 6000 I have seen this distorted chest in at least some dozen suffering from dyspnœa and bronchitis.* The finest specimens of the human thorax I have constantly seen associated with tubercular disease of the lung, and I believe that persons having this development are not materially less liable to phthisis than others." The experience at the Adirondack Cottage Sanitarium fully confirms this. Alison, however, goes on to say that the flat chest, which has been held to predispose to pulmonary tuberculosis, is the consequence of it, and the departure from the healthy or normal form may prove, especially where the acoustic signs are deficient, "an aid of some value and deserving of some reliance." In other words, careful inspection of the chest in pulmonary disease is of great value in many early cases.

Adirondack Cottage Sanitarium Data. Chest measurements have been taken at the Adirondack Cottage Sanitarium on and off for a number of years, but until February, 1901, the measurements were not taken in sufficient detail and exactness to be of much value. From time to time measurements of various parts have been added, until at present the following measurements are taken in all cases on admission and discharge (height on admission only): Height, girth of chest at level of the fourth† costal cartilage on quiet breathing, forced inspiration and forced expiration, length of chest, diameters of chest in a horizontal plane during post-expiratory pause (anteroposterior diameter, sternum to tip of spinous process; transverse diameter, over ribs, not in interspaces) at the level of the fourth

* This was written before the discovery of the tubercle bacilli.

† Since these measurements were taken the level of the juncture of the fifth costal cartilage and sternum is used.

costal cartilage and at the tip of the ensiform cartilage; the anteroposterior diameter at the top of the sternum, breadth of nipples, diagonal diameter in a horizontal plane from the vertebral spine to the right and left nipples.

In this investigation the diameters at the level of the fourth costal cartilage, the length of the chest in the midclavicular line parallel to the midline and the expansion (the difference at the fourth costal cartilage between the girth on quiet and forced inspiration), and the respiratory movement (the difference at the same level between forced expiration and forced inspiration) are the only measures considered. In considering change in the shape of the chest the diameters afford a means of comparison more accurate than the circumferences, on account of the increase of adipose tissue. It may be added that the patients at the Adirondack Cottage Sanitarium are drawn from all classes of society, from varied races, and from all parts of the continent, so that they are fairly representative of the general public and not merely of a class or section.

The Diameters, Length, and Index of the Chest in Males. The maximum of the anteroposterior diameter of the Adirondack Cottage Sanitarium cases is most marked at 18 cm. (See Chart I.) The normal anteroposterior diameter may be stated to be about 20.5 cm. When divided into stages the maximum of the cases at the Adirondack Cottage Sanitarium are:

Incipient	19 to 20 cm.
Advanced	18 cm.
Far advanced	18 cm.

The advanced cases have a marked submaximum at 20 cm.

The transverse diameters show a maximum at 25 cm. in the Adirondack Cottage Sanitarium cases, and at 24 cm. in the Brompton cases. The Adirondack Cottage Sanitarium cases treated as before give:

Incipient	27 cm.
Advanced	25 cm.
Far advanced	No definite maximum.

The normal transverse diameter is about 28 cm.

The normal chest index may be said to range between 72 and 75. The index of the Brompton cases was 80, that of the Adirondack Cottage Sanitarium cases 72. (See Chart II.) On separating the Adirondack Cottage Sanitarium cases as before, we get:

Incipient	69 and 72 cm.
Advanced	68 and 71 cm.
Far advanced	No definite maximum.

The far-advanced cases show a tendency to have a higher index than the others.

The length of the chest in the Adirondack Cottage Sanitarium cases seems slightly larger than that in the Harvard cases, while the Fort Porter and Brompton cases are much shorter. The incipient cases among the Adirondack Cottage Sanitarium cases seem slightly longer than the advanced. When compared with the height of the patient, more striking results are obtained. Fifty per cent. of the Harvard cases show a ratio of 19.1. The same proportion of the Adirondack Cottage Sanitarium cases show 19.9, and this in spite of the fact that the heights in the latter are inclusive of shoes, which seems to confirm the view that the consumptive chest is long relatively to the height of the person. The Brompton cases and those at the Adirondack Cottage Sanitarium who are far advanced show a much shorter chest.

The Chest in Females. The maximum for the anteroposterior diameter in females at the Adirondack Cottage Sanitarium was 18 cm., 1 cm. longer than the Sargent cases. This difference is probably largely due to age, as the Sargent group of cases are comparatively young. The transverse diameter, however, shows a maximum for the Adirondack Cottage Sanitarium cases at 24 cm., and Sargent's at 24.5 cm. The general tendency for both measures is for those of the Adirondack Cottage Sanitarium to be smaller than the Sargent cases, and this in spite of the difference in age. The incipient group shows a slight tendency to be a little smaller in both diameters.

There is no definite preponderance of any index type in the Adirondack Cottage Sanitarium cases, where the maximum is about 71.3 degrees higher than the index of the Sargent cases. (See Chart II.) The incipient cases have a maximum at 71, the advanced at 69, the far advanced at 71 to 74.

Nothing can be said in regard to the length of the chest in females, as there are too few measures upon which to base any conclusions.

Effects of Emaciation. To determine the effect of emaciation and consequent loss of musculature, a series of measures were taken in a number of emaciated cases whose lungs and heart were apparently normal. The number of cases found fulfilling these conditions were small, and the results are, therefore, inconclusive; but the facts obtained point to the conclusion that much change of index is not necessarily associated with emaciation. Eleven male cases had an average index of 71, 7 females of 73.4.

Changes in the Shape of the Chest during Sanitarium Residence. When considering the changes in the shape of the chest during Sanitarium residence various factors have to be taken into account. The average Sanitarium residence is about seven months, and during this period many patients undergo a marked change in health and general condition. A summary of the changes in measures between admission and discharge furnishes interesting results. (See Table II.)

TABLE II.—Changes in chest measurements during Sanitarium residence.

Sex.	Condition.	Anteroposterior diameter.			Transverse diameter.			Length.		
		Admission.	Discharge.	% increase.	Admission.	Discharge.	% increase.	Admission.	Discharge.	% change.
Male	Incipient	19.20	19.79	3.0	26.36	27.16	3.0	34.37	34.07	—0.9
"	Advanc'd	18.92	19.35	2.0	26.17	26.79	2.4	34.64	34.68	+0.1
Female	Incipient	16.86	17.25	2.0	23.61	24.01	1.7	33.54	33.34	—0.3
"	Advanc'd	16.96	17.47	3.0	23.69	24.58	3.8	33.94	34.04	+0.3

Both diameters of the chest show a clearly marked increase of 2 to 3 per cent., which is far in excess of what could be accounted for by the slight increase in age. These increases when considered as a whole show a tendency to be proportional to the diameters and do not alter the average index appreciably. The possibilities of the transverse diameter as to development appear to be much greater than those of the anteroposterior. If the cases showing an increase of index are grouped together and those showing a decrease, the averages of the two are markedly different. Moreover, when the cases are separated into several groups according to the index on admission, those groups with a low average index on admission show an increased index on discharge, while those with a high index on admission show a decreased index on discharge. So it appears that there is a reduction of the extreme indices at both ends of the scale (below 69 and above 80) and also a reduction in the number at the middle (about 72). There is a further tendency to gather around two index points, about 69 and 80, which appear possibly to represent two types of chest. From measures taken on admission and discharge in 130 males and 134 female patients, slightly more than 10 per cent. show changes of index of 5 degrees or more. Changes of 3 and 4 degrees are frequent. From this it would appear that the shape of the chest is easily modified within certain limits, and this conclusion is strengthened by the fact that the vast majority of cases show some change in the index. Further, it would seem that whatever the cause may be there is a very wide range to the index possibilities of the normal chest, from say 60 to 85. The elevation of 1600 feet has not been considered sufficient to produce much change from the rarefaction of the atmosphere.

The ratios of the chest diameters to the height of the individual are less in advanced than in incipient cases, and less again in the far advanced. The progress of the disease seems, therefore, to affect the diameters.

The most striking change is the increase in the expansion and respiratory movement. For comparison with Table III. the following figures are of value: Expansion (in millimetres) male: Yale,

49; Amherst, 48; Williston, 47; Cornell, 45.7. Female: Nebraska, 59; Mt. Holyoke, 48. Respiratory movement: Mt. Holyoke, 95.

TABLE III.—Changes in chest measurements during Sanitarium residence.

Sex.	Condition.	Expansion.				Respiratory movement.			
		Admission.	Discharge.	Difference.	% increase.	Admission.	Discharge.	Difference.	% increase.
Male	Incipient	4.46	4.84	0.38	8.6	8.92	10.38	1.46	16.1
"	Advanced	4.17	4.63	0.46	11.1	7.80	9.85	2.05	26.3
	Total	4.26	4.70	0.44	10.3	8.18	10.03	1.85	22.1
Female	Incipient	3.40	3.56	0.16	4 7	7.51	8.51	1.00	13.3
"	Advanced	2.96	3.25	0.29	9.9	6.34	8.41	2.07	32.7
	Total	3.12	3.36	0.24	7.9	6.73	8.44	1.71	25.5

Predisposition to Pulmonary Tuberculosis and Chest Index. To determine whether any particular chest index is especially subject to tuberculosis, two courses are open, both of which should give the same results. The first is to take the measures of a number of young people and see how they turn out in the course of say ten or fifteen years. This is almost impossible, and is subject, unless the number of cases is very large, to many sources of error, owing to the varying environments of the individuals.

The second method is to take a series of cases in the early stages of tuberculosis before the disease has had much opportunity to affect the shape of the chest (an important factor which acts more rapidly than is often supposed) and to compare them with a series of healthy individuals to see whether there is any difference in the proportion of cases at any of the indices. If a considerable difference is found in the frequency curves of the two series it may reasonably be concluded that there is some causal connection between index and disease, but, on the other hand, when the curves are practically identical, then it can as surely be considered that the shape as distinguished from the size is not a causative factor in the case. Comparisons of the frequency curves would seem to show slightly opposite results in the males and females; but, on the whole, the conclusion appears warranted that no one index of the chest can at present be said to be more liable to consumption than others.

In conclusion, it may be said that in attempting to formulate a standard for the dimensions of the chest it must be borne in mind that there is no absolute standard of human development. Each race has its own peculiarities, and in each race there is a wide range of divergence. It is about impossible to determine the normal type, as so many influences affect it. What is normal for one class is

extremely abnormal for another. This applies not only to the measurements themselves, but also to their relations to each other. Results in mass tend to gather around some central value which there is a great temptation to regard as a type, an end at which nature was aiming, but when further analysis is made, this value is found to vary from class to class and to have no existence in itself, but to be merely the result of the combination of several different series. For instance, the mean British stature of 67.66 inches splits up into English, 67.36; Scotch, 68.71; Welsh, 66.66; Irish, 67.90. These again could be subdivided into various classes with still further varying results. This seems to be especially true in any discussion of the chest index.

Comparison by the "Average" Method. The method of comparison in this article,which may be termed the "frequency method," yields, it is believed, as has been stated before, more accurate results than the method of "averages." However, it has been deemed expedient to give here the results obtained by the latter method. Table IV. gives the averages for each measure, the chest index, and the ratios of the anteroposterior and transverse diameters to the height of the patient. The smallness of the diameters in the Adirondack Cottage Sanitarium cases is real and not merely a consequence of the patients being small generally, as is shown by the ratios of depth and breadth of chest to total height of person, especially when allowance is made for the underdevelopment of the majority of the college men on account of their youth. Combining the Yale, Harvard, Fort Porter, Tufts, and Otis measurements in the male, the average anteroposterior diameter for the healthy chest is 19.1 cm., the average transverse diameter 26.7 cm., and the average index 71.4. For the consumptive chest the figures are 19.3 and 25.9 cm. and the index 74.6. For the female the normal figures are 17.64 and 24.85 cm., and 70.0; the consumptive, 17.1 and 23.7 cm., and 72.6. It must not be overlooked, however, that a greater part of the healthy chests included in these averages are young and not fully developed. This makes the average diameters less than the adult normal. The Yale cases, further, are more than two-thirds of the total, so that they have a preponderating influence on the results. That the difference between the average index of Dr. Hutchinson's consumptive cases and the Adirondack Cottage Sanitarium cases is so much greater than between the Adirondack Cottage Sanitarium and the average of all healthy cases obtained would seem strong evidence that the high index is a result and not a precedent of tuberculosis.

While studying the ratio of the chest diameter to the height by ages it was clearly shown that there is at first a marked decrease and later a marked increase of the ratios.

Relation of Race and Index. No definite relation seemed to exist between race and chest index in the data at the Adirondack Cottage Sanitarium, but the statistics on this are imperfect and admit of no

definite conclusions. On account of the influence of race on other measures of the body, it is probable that the chest index does not escape this influence.

TABLE IV.—Average of various series of chest measurements.

Sex.	Source.	Cases.	Antero-posterior diameter.	Antero-posterior ratio.	Transverse diameter.	Transverse ratio.	Index.	Length.
Male	Harvard	540	20.57	11.75	26.46	15.09	77.5	33.30
"	Yale	2300	18.70	10.84	27.00	15.66	69.3	
"	Tufts	102	18.50	.....	27.17	.....	68.2	
"	Otis	400	19.00	.....	25.10	.....	75.7	
"	Fort Porter	50	20.68	12.06	27.97	16.26	73.9	31.91
"	Brompton	40	20.32	.....	25.65	.....	79.6	31.50
"	Adirondack Cottage Sanitarium	249	19.08	11.04	25.93	15.22	73.8	34.28
Female	Sargent	180	17.64	10.89	24.85	15.13	70.0	30.00
"	Nebraska	....	17.00	10.62	25.10	15.69	67.7	
"	Adirondack Cottage Sanitarium	251	17.13	10.51	23.66	14.46	72.7	

Variation in Diameters and Index. The amount of variation in absolute measure required to produce marked changes in the chest index is small. One-half centimetre difference in the anteroposterior diameter makes about two degrees difference in the index, and a half centimetre in the transverse about one and one-half degrees. So a slight difference in both diameters makes a marked difference in the index. For future reference, it may be said that the anteroposterior diameter at the top of the sternum showed a maximum at 14 cm. and averaged 14.35 cm. At the level of the ensiform cartilage the anteroposterior diameter showed a maximum at 19 cm. and averaged 19.34 cm. For the transverse diameter at this level the figures were 26.5 and 26.39 cm.

Heredity and Index. To determine the effect of heredity upon the index, the cases with a tuberculous father or mother, or father and mother, 80 in number, have been studied separately. The cases are too few to base any definite conclusions upon, but the average index for the group was: male, 75.2; female, 72.4. The cases in which the mother alone was affected seemed to have a slightly higher index (75.5) than the average in the male patients, slightly lower (72.4) in the females. The figures vary so slightly from the normal average that no conclusion seems warranted.

Occupation and Index. The relation of occupation and chest index is of interest. The following are the indices for various occupations:

MALE.

Students	(19)	70.05
Clerks, etc.	(44)	72.07
Mercantile and trading	(25)	74.00
Manufacturing and mechanical	(25)	75.32
Farmers and outdoor workers	(18)	76.06
Professional classes	(26)	76.72

FEMALE.

Teachers	(27)	70.59
Manufacturing	(15)	72.60
Housework	(52)	73.11
Trained nurses	(23)	73.52

The lower index of the students and teachers may be partly explained by age. No explanation for the variation of index has suggested itself.

Many minor variations in the shape of the chest in pulmonary tuberculosis have been pointed out. Alison,[6] in 1861, showed that the sternum was flat, and Rothchild[7] has recently called attention to the fact that the Angulus Ludovici is less prominent than usual, and may, in fact, be obliterated. He, as well as Gee, has been unable to find any reference to this angle in Louis' writings, which upholds Conradi's contention that it is well marked in phthisis. He says at the junction of the manubrium and the gladiolus the second costal cartilage is often enlarged, forming a pyriform exostosis, suggesting an apparent increase in the angle. Mensuration proves that, as said before, it is decreased or obliterated and movement at the junction limited.

Freund[8] has stated that premature ossification of the first costal cartilage causes a diminution in the upper aperture of the chest.

Von Behring[9] has recently suggested that many children very early in life may have tuberculosis at the junction of the costal cartilages and the sternum, which may result in some deformity. No observations are adduced to uphold this theory.

While much attention has been given to the shape and the size of the bony structures of the thorax, the size of the lungs has received little or none. There is no inherent reason why an individual should not have a congenitally small or weak pair of lungs. What is true of the heart is probably true of the lungs. The shape of the bony thorax is easily changed within certain limits, and why the atmospheric pressure combined with a congenitally small lung volume should not cause a change in the shape of the chest is difficult to see. This, too, would seem to be a reason why the chest should not be rounder or deeper than normal, although a circumference in the form of a circle includes more space than in any other shape.

CONCLUSIONS. 1. The measurements of the normal chest up to this time have not been determined with sufficient accuracy to allow of very positive conclusions.

2. The influence of race, age, occupation, and altitude must be considered in determining the normal measures and relations. The chief impression gained from this study is that the chest, which is subnormal in its diameters and normal or supernormal in its length, is the chest more subject to pulmonary tuberculosis, though whether in many cases the disease liability and the shape of the chest are not both results of the same conditions and not casually connected, is an open question. Influences which tend to improve the develop-

ment of the chest tend also to prevent consumption, and this may account for the relative immunity of the well-developed chests.

3. The anteroposterior diameter in health may be stated to be about 20.5 cm. at the level of the nipples; the transverse about 28 cm., giving an index of 73. In the early stages of pulmonary tuberculosis the anteroposterior diameter at the level of the fourth costal cartilage is about 19.5 cm., the transverse about 27 cm., giving an index of 72. In advanced stages the figures are about 19 cm. and 25 cm., and index 76.

4. The female chest shows a tendency to a lower index than the male.

5. The chest index is readily changed within certain limits in the individual.

6. The influence of pulmonary tuberculosis has some tendency to reduce the diameters of the chest, and it seems as if it also reduced the length.

7. The progress of the disease probably tends to increase the index, though further data are necessary before this can be confidently stated.

8. There seems to be some tendency for the chest in pulmonary tuberculosis to acquire a larger or smaller index—*i. e.*, to divide into two types; one flat (index 68 to 70) and one deep and round (index 78 to 80), but both reduced in size.

9. Dr. Hutchinson's normal index appears to be too low, his tuberculous index too high. For far-advanced cases his tuberculous index is probably correct.

10. The relation of the diameters (*i. e.*, the index) does not appear to have any prognostic value, as at either extremes there is no tendency in early cases of pulmonary tuberculosis to show an unduly large proportion of extreme indices.

11. The change of index in pulmonary disease is probably not due to emaciation, but to change in bulk of the lungs.

12. During Sanitarium residence there is marked increase in both expansion and respiratory movement, more striking in advanced than in incipient cases.

This study would have been impossible but for the kindness of a number of our friends. Among them we wish to thank for the unfailing courtesy which they showed us Drs. Woods Hutchinson, D. A. Sargent, J. W. Seaver, Richard Dutton, and C. C. Stroud.

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PULMONARY STREPTOTHRICOSIS.

NOTES OF A CASE WITH CLINICAL PICTURE OF PULMONARY TUBERCULOSIS. SPUTUM CONTAINING AN ACID-RESISTING STREPTOTHRIX. NO TUBERCLE BACILLI.

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During recent years a number of observations have greatly advanced our knowledge concerning the genus *Streptothrix* and the pathology of streptothrix infections. Thirty or more species of streptothrices have been described and the cultural characteristics of the majority fairly well determined, so that some definite light has been thrown upon the confusion in which this particular group of micro-organisms has been involved.

Several points in particular appear to have been decided by this recent work. In the first place, a greater tendency toward unanimity in terminology has been shown. The terms *Actinomyces*, *Cladothrix*, *Oospora*, *Nocardia*, and *Streptothrix* have all been used as generic synonyms for branching mycelial organisms, but in the last two or three years a decided preference has been manifested toward discarding of the older terms in favor of the term *Streptothrix*. The majority of pathologists seem to be following this usage, though some prefer to cling to the older and more proper designation *Actinomyces*. But as *Actinomycosis*, instead of being a single disease-entity caused by a single micro-organism (*Actinomyces bovis*, Harz and Bollinger), has been positively shown to be a variety of infections due to different species of streptothrix, there are some very good reasons for abandoning the use of the term actinomycosis, at least in the pathological sense, in favor of the term *Streptothricosis*. The former term, though the older, can at present retain only a broad clinical significance as a designation for a class of diseases caused by related but distinct specific organisms.

Actinomycosis in man appears in the majority of recently reported cases to be due to other forms of streptothrix than the common one infecting cattle (*Streptothrix* [*Actinomyces*] *bovis communis*). Indeed, the cattle disease is most probably a varied infection caused by several species of streptothrix. Should the study of a greater number of cases prove this to be generally true, it should be more advisable not to designate these different infections by one and the

same clinical term. Still further ground is found for this in the fact that these different forms of streptothrix infections are not clinically identical, but present important differences in so far as symptoms, prognosis, and treatment are concerned. As to the designation of those streptothrix infections which are not caused by the common one of cattle under the head of pseudoactinomycosis or pseudotuberculosis, little need be said. There is a nearly general unanimity of opinion as to the impropriety of these terms. Manifestly at present the best way out of the difficulty is to class all streptothrix infections under the general heading of *Streptothricosis*, giving the specific name of the particular organism causing the infection. At the present time the cultural identification of the organism causing these conditions is of the greatest importance, and until this has been accomplished in a large number of cases we shall have little foundation upon which to base a definite clinical and pathological conception of these infections. With the accumulation of well-studied cases it is possible that some more satisfactory system of nomenclature may be devised.

Among the recently reported cases of human infection with streptothrices, there stands out prominently a small but exceedingly interesting group of pulmonary cases presenting the clinical picture of tuberculosis, bronchopneumonia, or gangrene, but in which the infecting agent appears to be some form of streptothrix differing from *Streptothrix bovis communis*. Not only have these cases been shown to be associated with different species of streptothrix, but they have also presented clinical and pathological characteristics quite different from pulmonary actinomycosis when caused by the cattle streptothrix. While there can be no doubt that pulmonary infections with the latter organism have actually occurred in man and have been correctly diagnosed, it is very probable, in the light of recent studies, that only a small proportion of the cases in man described as actinomycosis have been due to this particular organism.

Eppinger[1] isolated a streptothrix having well-marked cultural characteristics from a patient, a glass-polisher, aged fifty-two years, who had been treated for "cerebrospinal meningitis." Autopsy showed an abscess in right cerebral hemisphere which had discharged into the lateral ventricle, calcification of the bronchial and supraclavicular glands, old caseous nodules in apices of lungs, and a "pseudotuberculosis" of lungs and pleura. The streptothrix was isolated from the pus of the cerebral abscess. Inoculation of the pure culture into guinea-pigs and rabbits produced a "pseudotuberculosis." The organism was first designated *Cladothrix asteroides* by Eppinger, but has been since classed as *Streptothrix eppingeri* (Kruse). It does not liquefy gelatin or inspissated horse serum, and has no diastatic action on starch in peptone solution. On maltose agar the growth is at first of a yellowish-white color, then becomes

of a deeper yellowish to a yellowish-red. On potato the growth is at first whitish, then becomes of a yellow to a brick-red color, and shows a fine, powdery efflorescence on the surface. Reaction of alkaline litmus milk not changed after twenty days' incubation. Portions of the mycelium are acid-fast, but not alcohol-fast.

Sabrazés and Rivière[2] report 2 cases of human streptothricosis in which the lung was involved. In the first case a branching filamentous organism was found in the pus from cerebral and kidney abscesses in a young man, who also presented pulmonary abscesses. The organism, however, was not found in the latter. The organism stained with Gram's, and in anaërobic cultures produced white, cloudy colonies of streptothrix. In the second case a streptothrix was obtained in a pure culture from the sputum and the pus of subcutaneous abscesses. It was aërobic, liquefied gelatin, and produced a yellow pigment. It was not pathogenic to animals unless inoculated in association with lactic acid.

Buchholz[3] reports a case of a steel-worker, aged thirty-eight years, presenting the clinical appearance of tuberculous pneumonia and empyema. The sputum contained streptococci, but no tubercle bacilli. Autopsy showed extensive pleural adhesions, and empyematous cavities communicating with cavities in the lung tissue. These resembled tuberculous cavities, except in possessing more ragged walls. The tissue about the cavities was consolidated and presented necrotic and atelectatic areas. Microscopically the consolidated areas gave the appearance of a fibrinous pneumonia rather than of a tuberculous process. Staining with Gram's showed throughout the necrotic tissues around the cavities a thick network of delicate branching threads of about the same thickness as tubercle bacilli. The filaments showed occasionally interrupted staining, with here and there a thickening, but no coccoid or bacillary forms. Streptococci were not found in the infiltrated and necrotic parts, but were present in the atelectatic regions. Tubercle bacilli were not found. Buchholz, therefore, believes that the streptothrix was the cause of the lobular pneumonia and resulting necrosis, and that the streptococcus invasion was secondary. Cultures were not successful, the plates being overgrown with a variety of proteus. Animal experiments were not carried out. No mention is made of the staining properties of the organism as regards its acid or alcohol resistance. He regarded the organism as identical with or related to that of Eppinger.

Scheele and Petruschky[4] describe the case of a woman, aged fifty-six years, who, after an attack of influenza, developed a condition characterized by irregular fever, pain in the left side, and multiple subcutaneous abscesses, occurring particularly in the neighborhood of the joints. After three months' illness death occurred, and the autopsy showed left-sided pleuropneumonia, cardiac dilatation, splenic enlargement, cystitis, and pyelitis. From the sputum and

the pus of the subcutaneous abscesses there was obtained a streptothrix in pure culture, which, on agar, formed pure, white colonies, having a characteristic odor. Growth was also obtained on gelatin and in bouillon, but not on potato or on glucose agar. In the sputum the organism proved acid-fast when stained by Gabbett's method. This case is the first in which pulmonary streptothricosis was diagnosed during life.

Petruschky[5] refers to a second case in which a similar organism was isolated from the sputum of a child thought to have tuberculosis. This organism differed from that described above in giving a more abundant growth and causing liquefaction of the gelatin.

Rullmann[6] reports a case in which there was a localized lesion near the root of the right lung (bronchial gland?) associated with the presence of a streptothrix in the sputum, occurring in tough, yellowish-green masses, consisting of interlacing filaments in pure culture. Some of the filaments showed true branching. They stained well with ordinary bacterial stains and with Gram's. Pure cultures were obtained, the organism growing well on all ordinary media. On blood serum it formed chrome-yellow colonies; in bouillon a good surface growth with later turbidity. Aërobically on solidified egg-albumen it produced filaments; anaërobically rods with club-shaped ends like diphtheria bacilli. The cultures possessed a mouldy or earthy odor. Inoculation into various animals gave positive results, the organism being recovered from the lesions. Suppuration of the lymphatic glands was the most striking feature of the infection. Only the filamentous form was found in the inoculated animals.

In 1902 Rullmann[6] reports further observations upon the sputum of this case. In the expectorated granules the same organism was found, partly in pure culture and partly in association with other bacteria. On Loeffler serum it formed chrome-yellow cultures, in part whitish, and resembled diphtheria cultures. In the cultures the organism showed clubbed ends and true branching. Bouillon was not clouded. On gelatin the growth was slow. A skiagraph showed three circumscribed shadows at the root of the left lung (areas of induration?), pleural shadow and diminished diaphragmatic movement on right.

Flexner[7] has studied very carefully a case of pulmonary streptothricosis in a colored man aged seventy years, closely resembling Buchholz's case, both in the clinical history, morbid anatomy, and morphological characteristics of the organism found in the lesions. The clinical picture was that of pulmonary tuberculosis. No sputum was obtained. Autopsy showed partial consolidation of both lungs, with caseous and calcareous nodules and early stage of cavity formation. The pleura over the fresh foci of consolidation was covered with fibrin and studded with small hemorrhages. Over the peritoneal surfaces, especially in the omentum, numerous nodules resembling tubercles were found. Similar nodules were present in the

liver and spleen. The mesenteric glands were not enlarged, but on section showed minute tubercles. Microscopically the sections of the lungs showed a cellular exudate in part, and in part a fibrinous one. The alveolar walls themselves were infiltrated with polymorphonuclear leukocytes. These showed marked disintegration, in some areas to the extent of softening and cavity formation. Circumscribed nodules having the size, form, and appearance of miliary tubercles were present. They consisted chiefly of epithelioid cells; giant cells were not found. These were present, however, in the peritoneal nodules, which very closely resembled tubercles in their structure. Throughout the diseased areas there was found a filamentous organism often in convoluted masses. The branches were sometimes capped by a conical swelling. The filaments in part stained irregularly, giving a beaded appearance. Rarely they showed a tendency to break into small rods. In the peritoneal nodules the organism appeared more in the form of rods with a marked tendency to beading. The organism stained well with Weigert's modification of Gram's, and in section stained with Gabbett's method retained the carbol-fuchsin to some extent. Cultures and inoculations were negative. No tubercle bacilli were found, and the inoculated guinea-pigs showed no evidences of tuberculosis. Flexner styled the process *pseudotuberculosis hominis*, and the organism *Streptothrix pseudotuberculosa*. He regards it as probably identical with the one described by Buchholz; and the latter, after seeing Flexner's slides and comparing these with his own, regarded the two organisms as probably identical.

Foulerton[8] reports a case of an Italian woman, aged forty-six years, having a history of chest trouble for ten years. The symptoms had increased in severity during the two years immediately preceding admission. Abscesses were present in the left axilla and above the left clavicle, and there was a marked induration of the subcutaneous tissues about the left shoulder. In addition, there were physical signs of extensive disease in the thorax. Large numbers of streptothrix were present in the expectoration and in the pus of the subcutaneous abscesses. From the latter the organism was obtained in pure culture, but could not be positively identified with any previously described species of streptothrix. It was, therefore, classed *Streptothrix hominis* (Foulerton). On nutrient maltose agar it gave a slowly increasing, dry-looking, whitish growth, resembling that of tubercle bacilli. There was no growth on potato or gelatin. On horse serum there was a scanty growth, showing moderate pitting and no actual liquefaction. Diastatic action not tested. Not acid-fast in the one culture examined.

Norris and Larkin[9] have made a very thorough study of 2 cases of bronchopneumonia in man characterized by intense catarrhal and necrotic inflammation of the bronchi and by the presence of numerous streptothrix colonies in the bronchial lumina. Inocula-

tion experiments were positive, and from the empyema pus of a rabbit inoculated from Case II. the streptothrix was finally isolated in pure culture. The organism was grown with great difficulty; solid media, with the exception of rabbit's kidney, being found unsuitable. When finally obtained, the colonies on neutral or 0.5 acid agar were of small size, whitish, and opaque, resembling more nearly bacterial growths than the dry growths characteristic of the streptothrices. On coagulated ascitic serum containing broth and sugar and on Loeffler's serum, a scanty, whitish growth was obtained. In bouillon two varieties of growth were obtained, one with small, hard, and adherent discoid granules, the other of the large, clumpy variety. No growth could be obtained upon potato. The organism stained with Gram's. When stained with hot carbol-fuchsin and decolorized in 97 per cent. alcohol, certain portions retained the red. With weak solution of acids the decolorization was complete. The authors regard their organism as probably identical with or at least closely related to *Streptothrix israeli*, or to the species isolated by Kruse. The pulmonary lesions of these cases, however, did not resemble the bronchopneumonic type of pulmonary actinomycosis described in the literature. The intense necrotic inflammation of the bronchi in the 2 cases distinguished them from previously reported cases of pulmonary actinomycosis or pseudo-actinomycosis.

Aoyama and Miyamoto[10] have reported a case of pulmonary streptothricosis in which the sputum and the pus from a cavity in the lung contained branched threads, which they described as being "as acid-fast as tubercle bacilli." From the pus in the lung cavity a pure culture of streptothrix was obtained. It stained by Gram's and by Gabbett's methods, the threads not staining equally, but portions remaining unstained. Anaërobically the growth was very scant. On glycerin-agar the developing colonies were whitish; in older colonies the centre was dark, opaque, and yellowish, with a thinner, whitish margin. On blood serum the growth was scanty and of a yellowish color. In bouillon fine, grayish-white, chalky colonies appeared on the surface; these became coherent and sank to the bottom as a flocculent precipitate, having a mother-of-pearl sheen. In old cultures the broth took on a brownish tinge. On potato the growth was at first white, but after a time became brownish, forming a loosely friable mass. Inoculations were positive; grayish-white nodules containing the streptothrix were found in the lungs, heart muscle, kidneys, spleen, brain, and on the peritoneum of the experimental animals. In a pregnant guinea-pig the organism was recovered from the blood of the placenta. The very full account given of this organism by Aoyama and Miyamoto makes it highly probable that it is identical with *Streptothrix eppingeri*. They themselves regard it as probably identical with the one described by Buchholz, but as the latter organism was not isolated, an absolute

identification becomes impossible. To the organisms described by Petruschky and Rullmann it has no resemblance.

Aoyama also states that in 1899 he had made an autopsy on a body dying of a condition diagnosed during life as tuberculous hemorrhagic pleuritis and kakke. In the hepatized portion of the lung numerous streptothrices were found.

Musser[11] reports a case of pulmonary streptothricosis in a man, aged thirty-seven years, suffering from bronchial symptoms and fever, and dying finally from bronchopneumonia. There was no leukocytosis, the leukocyte count being 3200. Streptothrical filaments and streptococci were found in the sputum. No cultures were obtained. The author was unable to decide whether the case was one of primary streptothrical infection or of primary streptococcus infection with secondary streptothrix infection, or whether the organisms described were branched tubercle bacilli.

Mayer,[12] in his "Briefe aus Ostasien," mentions 10 cases having pronounced symptoms of tuberculosis in which an acid-resisting and moderately alcohol-fast streptothrix was found in the sputum, pleuritic fluid, and in smears and sections from the pulmonary foci. He regarded these organisms as having the same significance as the acid-resisting bacilli found in pulmonary gangrene by Fraenkel, Pappenheim and Rabinowitsch.

Ohlmacher[13] describes an atypical acid-fast and alcohol-fast organism obtained from the sputum of a case clinically resembling pulmonary tuberculosis. Cultures could not be obtained, and inoculation experiments were negative. The inoculated animals showed no evidences of tuberculosis. The morphology of the organism as seen in the stained specimens of sputum corresponded neither to the tubercle bacillus nor the smegma bacillus, but was somewhat suggestive of Flexner's *Streptothrix pseudotuberculosa*, except in being a much more delicate organism. The author was unable to classify it, but was inclined to place the organism with the cases of Pappenheim, Fraenkel, and Rabinowitsch, in which acid-resisting bacilli resembling the tubercle bacillus were found in association with the pathological picture of chronic bronchitis and pulmonary gangrene.

Birt and Leishman[14] isolated a new streptothrix from the sputum and pleural effusion of a young man suffering from hectic fever and right-sided pleuritis, attended by the expectoration of a mucopurulent material. Autopsy showed an advanced empyema on the right side and a condition of chronic bronchopneumonia. Throughout the lung there were numerous small, hard nodules, showing no caseation and differing in many respects from miliary tubercles. The streptothrix was obtained in pure culture from the pericardial fluid and in connection with pyogenic organisms from the empyema pus and the nodules in the left lung. It grew very slightly at room temperature. In the incubator it grew rapidly on gelatin without liquefaction. On agar the growth was rapid, forming a

snow-white, dry, powdery material, taking on a pale coral-pink tinge after a few days. On potato a growth was obtained resembling a splash of plaster of Paris. There was no growth on blood serum. With Gabbett's method the organism was acid-resisting. It occurred both in branching threads and in the streptococcoid form. Inoculation showed it to be pathogenic for guinea-pigs.

Ophüls[15] reports 5 cases of pulmonary gangrene in which acid-resisting bacilli were found. True branching forms were found in all cases. Pure cultures were not obtained, and animal experiments were not carried out. It was impossible to decide whether the organism in all cases belonged to the same species. The author believed that they were certainly closely related and probably belonged to the class of acid-resisting bacilli found in butter, on timothy grass, etc. He would, therefore, class his cases with those reported by Fraenkel, Pappenheim, Rabinowitsch, Benvenuti, etc. He further suspects that the acid-proof bacilli come from the mouth.

Of the cases abstracted above, it is very probable that those of Mayer, Ohlmacher, and Ophüls belong to a separate class and are to be put by the side of the cases of acid-resisting bacilli reported by Fraenkel, Pappenheim, Rabinowitsch, etc. It is also a question if the organism described by Norris and Larkin may not also belong to this class. The authors themselves regarded it as closely related to *Streptothrix israeli*. The meagreness of description in Musser's case and his own doubt as to the character of his organism make its classification impossible. Of the other cases, Buchholz regarded specimens of Flexner's streptothrix as identical with his own, which he thought might be the same as Eppinger's. Aoyama and Miyamoto regard theirs as probably identical with the one of Buchholz; but Foulerton thinks from their very full description that it is identical with *Streptothrix eppingeri*. If we take the morphological descriptions alone the organisms of Buchholz, Flexner, and Aoyama and Miyamoto certainly fall into the same class. The failure of cultivation in the cases of Buchholz and Flexner make the final classification of their organisms impossible. On the other hand, the organisms described by Sabrazés and Rivière, Scheele and Petruschky, Rullmann, Foulerton, and Birt and Leishmann are distinct from *Streptothrix eppingeri* and probably from each other. It is apparent then that a variety of streptothrices are concerned in pulmonary infections, but that it is impossible at the present time to classify these definitely, either according to their morphological and cultural characteristics or from a pathological or clinical standpoint.

Such being our state of knowledge upon this subject, the report of every case of pulmonary streptothricosis observed becomes an imperative duty at this time. We add, therefore, to the casuistics of this subject the following case, which, though incomplete, lacking culture and inoculation experiments and autopsy, is of great importance in confirming the cases of Buchholz and Flexner, and in

showing the wide geographical distribution of this form of pulmonary streptothricosis:

HISTORY OF CASE. (Furnished by Dr. King, of Pueblo, Colorado.) —Mr. J. B., Austrian by birth, aged forty-five years, came to this country when a child and has since lived in Southwestern Kansas. He is married and has several grown children. No family history of tuberculosis. The patient has worked as a farmer for the greater part of his life, and, while never appearing especially robust, has been wiry and a hard worker. Three years ago his present trouble began with an attack of "la grippe," after which a moderate cough and expectoration persisted. In consequence he gradually became much weakened and emaciated, and suffered so much from digestive disturbances that he was finally compelled to live upon milk diet alone. In spite of his increasing weakness, he kept at work until six months ago, when he gave up completely and was sent to Colorado with the clinical diagnosis of tuberculosis.

The physical examination (Dr. King) showed good and symmetrical expansion on both sides. No areas of dulness were present and no signs of cavities. The respiration was labored, and on auscultation blowing breath sounds and dry crepitant rales were heard all over the chest. The sputum was raised with difficulty. It was mucopurulent in character, yellowish, and had no disagreeable odor. There was no fetid odor to the breath. The temperature ranged from 102° to 103°. The clinical picture on the whole suggested a chronic bronchitis or bronchopneumonia of tubercular origin.

The sputum was collected and sent to Dr. Olney for examination for tubercle bacilli. The specimen consisted of about one ounce of a yellowish-gray, nearly homogeneous, and somewhat gelatinous sputum, containing great numbers of minute grayish granules. It was easily spread, not stringy, but inclined to make rather thick smears. No blood streaks were seen in it, and it had no noticeable odor. The small grayish granules became more prominent in the dried covers. On the examination of the unstained fresh sputum, it was found to be moderately rich in pus cells. No yellow elastic tissue was found. No blood or pigment cells were present. The small grayish granules proved to be masses of a filamentous organism closely interwoven and branching freely. In the covers stained with carbol-fuchsin Dr. Olney was surprised to find that the branching threads would retain the stain after treatment with 25 per cent. of sulphuric or nitric acids, but gradually lost the red when washed in 95 per cent. alcohol. With the acid alone they were "as acid-fast as the tubercle bacillus." With Gram's the branching threads stained beautifully, standing out in sharp contrast against the clear background.

The unusual character of the organism was at once recognized by Dr. Olney, who suspected that the case was one of actinomycosis.

He therefore made a careful search for characteristic "Drusen," but failed to find anything at all resembling these. A very thorough search was also made for the tubercle bacillus, but none were found. With the exception of a very few streptococci and staphylococci, the only constituents of the sputum were the filamentous organism and pus cells. Convinced, therefore, that the case was one of infection with some rare member of the streptothrix group and not having access to the literature, Dr. Olney sent his preparations to the Pathological Laboratory of the University of Michigan for diagnosis. In the mean time, he at once made arrangements for securing cul-

FIG. 1.

Small grayish mass from sputum, consisting of tangled streptothrix threads, puss cells, etc. × 300.

tures, but, unfortunately, the patient had suddenly become much worse, and had been taken by his friends to a tuberculosis sanitarium, where he died on the second day after the first sample of sputum had been sent to Dr. Olney. No autopsy was permitted. No history of the case was taken at the sanitarium, nor was any examination of the sputum made there.

The specimens received from Dr. Olney consisted of smears of sputum stained with carbol-fuchsin (acid decolorization) and by Gram's method. In every field there was present a filamentous organism showing true branching. Usually the threads were

entangled, interwoven masses somewhat convoluted, but occasionally single branching filaments were seen. The filaments varied in length, but many extended across several oil-immersion fields. The length of the branches also varied greatly, but the majority were short. No conical or club-shaped terminations were seen. The filaments also varied in thickness, the majority being about four times as thick as a tubercle bacillus, though some threads had about

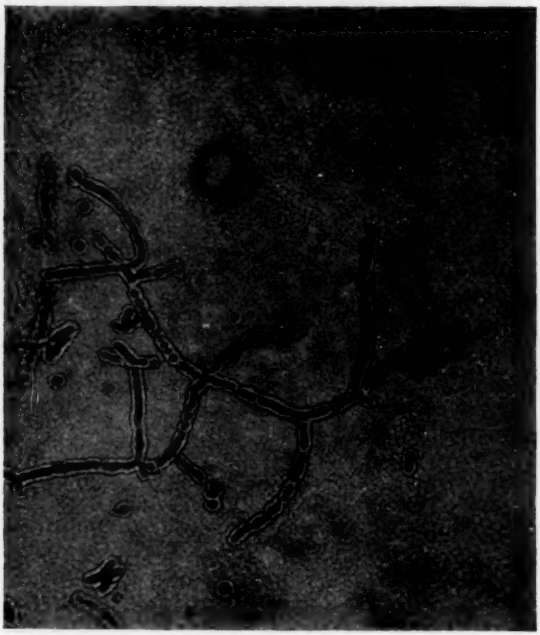
FIG. 2.

Mass of streptothrix threads from sputum, stained with carbol-fuchsin and decolorized in 25 per cent. nitric acid. All the threads acid-fast. × 750.

the same thickness as the latter. No bacillary or coccus-like forms were found. In the specimens stained with carbol-fuchsin and decolorized with acid, the majority of the threads presented a beaded appearance or seemed to be breaking up into short rods of varying length. The staining of the beaded threads is very irregular, and the beaded appearance seems to be dependent upon the degree of decolorization. The deeply staining threads are wider than the lighter ones, and by focusing a clear unstained protoplasm may be

seen connecting the stained portions. The unstained portions are somewhat wider than the stained. In the smears stained with Gram's the beading is not so marked, although by longer decolorization it becomes more evident. It would seem, therefore, that the beading is more or less dependent upon the staining procedure. Pus cells were found in moderate numbers in the mesh of threads, many mononuclear cells being present. Streptococci and staphylococci were present in small numbers.

FIG. 3.



Streptothrix threads from sputum, stained with carbol-fuchsin and decolorized in 25 per cent. nitric acid, showing true branching and beading. × 1200.

From the above characteristics it was at once evident that the organism was a streptothrix, morphologically identical with the ones described by Buchholz and Flexner. This opinion was confirmed by Dr. Flexner, to whom stained smears were shown. There can, therefore, be but little doubt that this case was one of pulmonary streptothricosis, even in the absence of autopsy confirmation, and that it is to be classed with those of Eppinger, Buchholz, Flexner, and Aoyama and Miyamoto. In the absence of definite knowledge

concerning the cultural characteristics of the organism in the cases of Buchholz and Flexner, as well as in our own, no absolute identification of the species of streptothrix is possible, but it seems very probable that in all of these 5 cases either the *Streptothrix eppingeri* or a very closely related species is to be regarded as the cause of the infection.

We must conclude, therefore, from these 5 cases that there is a distinct form of pulmonary infection clinically resembling tuberculosis and caused by an acid-resisting streptothrix having a wide, geographical distribution. The existence of such a condition becomes of great importance, in so far as the question of the differential diagnosis of tuberculosis is concerned. The frequency of occurrence, the symptomatology, and the therapeutics of this form of streptothricosis remain yet to be worked out, and it is highly desirable that those happening to meet such cases should make a thorough investigation as to these points and also as to the cultural characteristics of the infecting organism.

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TUBERCULOSIS AND HEART DISEASE.

BASED UPON THE STUDY OF 1764 AUTOPSIES, 1276 CLINICAL HISTORIES, AND A REVIEW OF THE LITERATURE.

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Having within the last year had the opportunity of examining all the post-mortem records at three of the hospitals in Philadelphia, aggregating a total of 7040, I have collected data from all those which showed tuberculous lesions of the lungs, pleura, peri-

cardium, heart, and great vessels, with a view of studying their frequency and relationship.* Statistics have also been gathered upon 57 successive cases of valvular heart disease which have come to autopsy at the Pennsylvania Hospital. The individual totals from the different hospitals are summed up as follows:

	Total autopsies.	Tuberculous cases.	Per cent.
Philadelphia Hospital	6426	1606	26
Pennsylvania Hospital	562	106	18
Phipps Institute	52	52	100
	7040	1764	

Tuberculous pericarditis has been considered in a previous paper,† and will be omitted from the present one; it may be stated, however, that the condition is a relatively common one, it having been encountered 81 times in 1780 (4.4 per cent.) tuberculous autopsies; while in 31 additional cases of undetermined etiology tuberculosis may have been the causative factor. Small localized areas of inflammation—milk spots—were not included in the foregoing enumeration.

The earliest work dealing with the relationship of pulmonary tuberculosis and heart disease which I have been able to find dates back to 1806, the year in which Corvisart in his essay "On Diseases of the Heart and Large Vessels" described the existence of small hard tubercles situated on the mitral valve. But the subject did not attract much attention until Rokitansky, in 1846, first enunciated the doctrine of antagonism between valvular heart disease and tuberculosis of the lungs, claiming that the existence of chronic endocarditis virtually precluded the latter disease, and explaining this immunity by the congestion and stagnation of venous blood in the lungs.

Following out this line of thought Rokitansky[12] and his disciples taught that valvular disease of the heart, especially when affecting the mitral or aortic valves, as well as aneurysms of the large vessels, hydrothorax, and even scoliosis, lessened the tendency to pulmonary tuberculosis. This idea that scoliosis conferred a relative immunity is interesting in the light of modern research, especially in connection with preventive inoculation. The increased resistance to tuberculosis in individuals with scoliosis probably exists, not by reason of venous stasis, but because patients who have recovered from an attack of tubercular bone disease have usually developed an inhibitory capacity to tuberculosis of considerably greater potency than that possessed by an unaffected organism. Certainly it would seem to be an established fact that patients of the so-called scrofulous class often show an increased resistance to tuberculosis, which

* I am indebted to Drs. Biggs and Longcope, respectively, for having placed at my disposal the autopsy records of the Philadelphia and the Pennsylvania Hospitals.

† University of Pennsylvania Medical Bulletin, 1904.

if it gains foothold in the economy often runs the protracted course of a disease implanted upon an unfavorable soil.

Rokitansky's doctrine held unchallenged sway until Traube,[13] in 1864, reported a series of cases in which aortic disease and phthisis pulmonalis were coincidently found at autopsy. The last-named author, however, admitted the extreme rarity of such coincidence, but believed that mitral stenosis was directly inhibitory. Three years later corroborating though modifying evidence was added to the antagonism doctrine, when Lebert[14] reported 24 cases of pulmonary stenosis (15 in men, 9 in women), all of whom were the subjects of pulmonary tuberculosis, and most of whom died of the latter disease without having a tubercular heritage, before reaching the age of twenty-five. If Rokitansky's views were correct and venous stagnation prevented tuberculosis, it seemed but natural to believe that the anæmia of pulmonary stenosis should favor it.

It was not until 1875 that the antagonism theory received undeniable disproof. In this year Frommolt,[15] in a paper based upon 7870 autopsies made in Dresden in the course of twenty-five years, reported 277 (3.5 per cent.) cases of valvular heart disease—all but 1 lesions of the left heart—among which 22, or 8 per cent., had pulmonary tuberculosis. Following the footsteps of Frommolt, Niemeyer, Ruehle, Lepine, and others adduced corroborating evidence and succeeded in quite thoroughly discrediting the absolutism of Rokitansky's teaching, although many authorities still insist on the rarity of coincident tuberculosis and disease of the heart. Certainly the trend of modern belief is to set but little if any faith in the immunizing effect of chronic endocarditis, a fact which is no doubt due largely to the increasing accuracy and thoroughness of our pathological research.

Another belief held by Rokitansky, and before him by Laennec,[111] Louis,[112] and Bizot,[16] was that pulmonary tuberculosis usually if not always occurred in individuals with small hearts. Louis, in 112 autopsies upon tuberculous individuals, found the heart enlarged only three times; in about one-half of the cases it was subnormal in size. Beneke[1] met with similar results in a large number of cases, and believed the condition to be due to a congenital hypoplasia, in which the vascular system shared. Potain,[2] while admitting the fact, attributed the smallness of the heart to impoverished nutrition. Reuter,[3] in a series of 251 autopsies, encountered the following state of affairs:

Small hearts	men	29.0 %
	women	56.0 %
Normal hearts	men	30.7 %
	women	28.2 %
Large hearts	men	40.2 %
	women	20.0 %

Hirsch,[4] on the other hand, found the heart enlarged in 44 per cent. of his tuberculous cases, and abnormally small in only 5 per cent.,

the increased size being due to an hypertrophy of the right ventricle. The doctrine that cardiac hypoplasia was a potent factor in the predisposition to tuberculosis was enthusiastically heralded by Brehmer,[5] who was impressed with this belief by observations made upon the inhabitants of Goerbersdorf—a mountainous resort in which rarefied air conduced to hypertrophy of the heart—among whom tuberculosis was extremely rare. Brehmer believed that the small heart of tuberculous individuals was the result of malnutrition during the period of growth, a condition which is evinced by the poor appetites of scrofulous children, who as a result do not attain a normal body weight. He tried to substantiate his dictum by the results of investigations which had been made upon growing animals, it having been shown that strong, well-fed, healthy oxen possessed smaller lungs in proportion to their body weight than did the less robust specimens, in which the hearts were relatively smaller in comparison to the lungs. Spatz[6] has collected statistics from 327 tuberculous autopsies in which the relative size of the cardiac orifices, wall, and chambers were carefully recorded. He found the heart in the majority of instances smaller than normal, with a tendency to left ventricular hypertrophy. The aorta was often found subnormal in calibre, especially in women. One case in the present series derived from the records of the Pennsylvania Hospital showed congenital atresia of the aorta, which had been found in an adult negro who died of pneumonia and who had never been conscious of cardiac insufficiency. The systemic circulation had been carried on through a patent and enlarged ductus arteriosus; there was no evidence of pulmonary tuberculosis. Oppenheimer's[7] studies showed that the greatest disproportion between the human heart and body existed at the time of puberty, a time when tubercular manifestations are very common. When enlargement of the heart is found in pulmonary tuberculosis it is often due to the use of alcohol (Bauer and Bollinger,[8] Reuter[3]) or to a coincident nephritis, it being therefore more frequently encountered in men. A more recent study of this subject has been made by Bouchard and Balthazard,[9] who have estimated the size of the heart in 90 living cases of pulmonary tuberculosis by means of the fluoroscope and radiographic screen which is held at different angles to the body. The results thus obtained were compared with: (1) the bodily height; (2) the frontal size of the thorax; (3) the weight of the individual; (4) the "fixed albumin" before emaciation, *i. e.*, the weight which a person of the same age, size, and musculature would have under normal conditions. The results of these investigations showed two classes of consumptives: 1. Those who had contracted tuberculosis, though not predisposed. 2. Those who were predisposed. In the first class the heart was normal in size; in the second, this organ possessed only one-half of its natural proportions; in other words, the heart had 0.5 sq. cm. less area for every kilogram

of fixed albumin than would have been the case in a normal individual. In the third stage of pulmonary tuberculosis this standard was raised through cardiac dilatation, the increase in size being indicated by about 10 sq. cm. in the total area as compared with the early stages of tuberculosis. In other chronic diseases this smallness of the heart was not found. Regnault[10] denies that the heart is atrophied in chronic pulmonary tuberculosis, and calls attention to the frequency with which dilatation or hypertrophy of the right ventricle is encountered. Fraenkel[11] comments upon the fact that this right ventricular dilatation is occasionally more easily demonstrable during life than at autopsy, and suggests as a reason the fact that during the last stages of the disease the blood pressure is lowered and the whole volume of the blood decreased. In the present series of cases the weight of the heart was recorded in 1269; it was found to be enlarged, *i. e.*, weighed over 380 gr., 217 times; in 161 of these the enlargement was associated with and presumably due to valvular disease or pericardial adhesions. The remaining 56 instances of hypertrophy were in a considerable number of instances apparently due the coincidence of chronic nephritis. The exact location of the cardiac enlargement was not regularly recorded, but such information on the subject as was obtainable resulted as follows: general hypertrophy, 41; right-sided hypertrophy, 20; left-sided hypertrophy, 38. The heart of adults was found to weigh less than 200 grams in 184 instances, leaving 707 normal-sized hearts. Hypoplasia of the aorta was met with three times. The following pathological cardiac conditions were also encountered in the 1764 tuberculous autopsies:

Brown atrophy	37	Gumma of lung	1
Fatty degeneration	24	Carcinoma of lung	1
Valvular fenestration:		Acute hemorrhagic myocarditis	1
Aortic	5	Tuberculosis of the aorta	1
Pulmonary	2	Tubercles on endocardium	5
Patulous foramen ovale	4	Tuberculous endocarditis	2
Abscess of mitral leaflet	1	Tuberculous myocarditis	6

The foregoing figures show that cardiac hypoplasia occurred with but moderate frequency; but it must be borne in mind that the majority of the cases were taken from the records of a hospital in which a large number of the autopsies are made upon individuals who have passed middle life, among whom syphilis and nephritis are common, who die in the almshouse or in the insane wards, with tuberculosis, it is true, but not necessarily of it. The post-mortem examinations at the Phipps Institute, where the majority of the patients are not beyond middle life, showed a very much lower proportion of enlarged hearts. It would seem, therefore, that in uncomplicated cases of pulmonary tuberculosis the heart is subnormal in size in quite a considerable number of the cases. A fact which must, however, not be lost sight of in this connection is that the heart of tuberculous individuals is often small not as the result

of hypoplasia, but from atrophy or degeneration of its substance. This fact has long since been sufficiently pointed out by Louis, Andral, Kidd, Bennet, Quain, Strümpell, v. Leyden, and has been observed by all who have given attention to the matter.

The clinical histories of the Phipps Institute show that among 1276 cases of pulmonary tuberculosis examined, dilatation of the right ventricle was demonstrated in 46. Jaccoud found this condition most frequently associated with large cavities in the lungs. Lebert[108] encountered hypertrophy of the right ventricle in 21 per cent. of the chronic and 13 per cent. of the acute cases.

Taking up Rokitansky's doctrine of immunity—or at least the modified view of it—that of a relative inhibition upon tubercular infection of the lungs—let us see upon what scientific facts such a resistance can be based. Congestion of the lungs when long standing produces an increased dilatation and tortuosity of the capillaries, causing them to project into the alveoli, which in turn brings about an increased transudation of serum. Following upon this, cell proliferation, with slight hypertrophy of the fibrous and muscular tissue, takes place, this being accompanied by an increased deposition of pigment. Here at once we have several causes at work which might inhibit tubercular growth. First, the increased transudation tends to wash out foreign bodies from the bronchioles, also favors cell nutrition and exercises a germicidal effect. Second, fibrous hyperplasia is in itself more or less inhibitive and destructive to tubercle bacilli. This is shown by the clinical course of fibroid tuberculosis, and by the fact that lungs with high grades of emphysema hardly ever show extensive tubercular involvement. Third, the addition of muscular tissue permits more forcible expulsion of extraneous material. "I think it not unlikely that this increase of contractile power may underlie the well-known immunity of the lungs affected with brown induration for such disorders as have their origin in the retention of retained catarrhal secretions." (Rindfleisch.) Based upon this idea that venous stagnation was unfavorable to the growth of the tubercle bacillus, Bier[17] was led to attempt the cure of tuberculous arthritis by means of an artificial stagnation of blood brought about by tightly bandaging the extremities on the proximal side of the lesion. Pearce[18] has lately called attention to the hypertrophy of the elastic fibres in the pulmonary tissues, which occurs in chronic congestion. The latter finding corroborates Hess'[105] contention that the amount and functional efficiency of the pulmonary elastic tissue plays no small part in the resistance of the organism to tuberculosis, the character and extent of the difference in the elastica of contrasted individuals being shown by the very variable degree with which this substance takes certain stains or decolorizes. Fossier,[115] on the other hand, has shown that tubercle bacilli are by no means rarely found in parts of the lungs which are most involved by cyanotic induration.

A search into the voluminous literature of the subject reveals marked differences of opinion and great discrepancies in the statistics. With one accord, however, all authors agree that stenosis of the pulmonary orifice favors the development of tuberculosis of the lungs. This predisposition was first pointed out by Frerichs. His claim was, as has already been stated, placed upon a firm basis by Lebert,[14] and later by Stoelker.[20] The former believed that the results were brought about, not owing to the pulmonary anæmia, as was taught by v. Leyden,[21] but by means of the abnormal and unequal character of the circulation. Fischer[22] attributes the frequency of tuberculosis to the general lack of vitality and resistance which is but to be expected in individuals with congenital malformations. The idea that tubercular infection in these cases was favored by pulmonary anæmia is manifestly erroneous, since the lungs receive their nutrition from the bronchial arteries. The frequency with which pulmonary stenosis is complicated by tuberculosis of the lungs is shown by the following tabulation of collected statistics:

	No. cases of pulmonary stenosis.	No. with pulmonary tuberculosis.
Louis	7	3
Rokitansky	24	10
Gintrac[107]	16	4
Lebert	24	15
Stoelker	116	16
Paul[23]	27	16
Scheele[108]	61	15
v. Carriere[109]	8	4
Peacock[24]	12	12
Schultze[25]	6	5
v. Kryger[26]	2	2
Meisenburg	5	4
Vierordt[110]	83	30
K. v. Ruck[29]	10	10
Babcock[100]	1	1
Burke[104]	47	18

Vierordt has called attention to the fact that the frequent occurrence of tuberculosis is not limited to pulmonary stenosis alone, but is noted also in other varieties of congenital heart disease. This author does not believe that pulmonary tuberculosis is any more frequent in pulmonary stenosis or atresia than is the case in other conditions in which the nutrition is profoundly impaired.

Much diversity of opinion has existed upon the relationship of mitral stenosis to pulmonary tuberculosis. Traube and Lebert held that this form of valvular disease had a distinctly inhibitory, almost immunizing, effect upon pulmonary disease. Teissier,[39] who has written an elaborate monograph upon the subject, denies these statements, but believes that the presence of this form of cardiac lesion favorably influences the course of the pulmonary disease. Similarly to Rokitansky, Potain, Renault, Fraenzel,

Friedreich, Ruhle, Lepine, and others, he attributed this state of affairs to the venous congestion. According to Peter,[30] this modifying influence is brought about by increased functionation of the pulmonary apices which occurs when the bases are congested. It has been suggested by Fischer[22] that mitral stenosis is less frequently encountered in pulmonary tuberculosis, because the duration of life in these cases is, by virtue of the cardiac lesion, necessarily a short one. This is an unsatisfactory explanation, however, because individuals with a double mitral lesion have an equally short, if not shorter, span of life, and yet the two diseases are more frequently coincident in the latter instance than in the former. Meisenburg[27] holds that when mitral stenosis and tuberculosis occur together the former is practically never primary. Fagge[31] states that the last-named variety of heart disease is almost a complete bar to tubercular infection, the statistics of Guy's Hospital having shown only four such cases in a period of thirty years. Walsham[32] found one case of mitral stenosis in 130 tuberculous autopsies, but failed to find this condition in 1000 clinical examinations. The same author in 91 cases which were clinically instances of pure mitral stenosis encountered 3 in which the physical signs might have been those of pulmonary tuberculosis; he does not believe that any definite relationship between the two conditions exist. In Frommolt's statistics of tuberculous cases, mitral stenosis occurred in 5 per cent.; mitral insufficiency in 10 per cent. of the cases. Potain[34] collected 55 instances of mitral stenosis from the autopsy records of the Necker and Charité Hospitals, covering a period of fourteen years, 9 of which showed tuberculous lesions in the lungs. Harris and Beale[33] found mitral stenosis three times in 133 tuberculous autopsies. Fraenkel[11] saw two cases of high-grade mitral stenosis which in the latter stages developed widespread tuberculous lesions in the lungs. Paliard[41] has reported a case of mitral stenosis of rheumatic origin, and of ten years' duration; the patient developed and rapidly died of pulmonary tuberculosis.

A glance at the following tables will show that the coincidence of valvular heart disease and pulmonary tuberculosis is encountered with only moderate infrequency; also that the condition has been more often recorded by recent than by older observers. Clinically the occurrence of valvular lesions has in some instances probably been overestimated, the murmurs heard having been due to other causes than to organic endocardial disease, and the symptoms of apparent cardiac insufficiency to the general systemic weakness, in which the heart muscle shared. On the other hand, slight grades of valvular incompetency are apt to be overlooked at autopsy, especially when the mitral orifice is involved. Varying degrees of endocardial thickening in which the valves take part is a very common finding in chronic tuberculosis; but this condition by no

means necessitates imperfect functionation. In the present series of cases endocardial thickening was found in 15 per cent. of the cases with the following proportion of valvular involvement: mitral, 183; aortic, 126; tricuspid, 23; pulmonary, 13. These cases were not included in those tabulated as valvular disease, among which only such lesions were considered which had been definitely designated by the pathologist as "insufficiency," "stenosis," etc. Teissier found sclerotic endocarditis in 40 per cent. of his tuberculous cases after excluding those which had had other infections. This induration of the endocardium may be generalized, but is usually more marked at the line of valvular contact or at that point of the endocardium at which these structures impinge during diastole. These lesions are most frequently seen on or in the neighborhood of the mitral valve.

CLINICAL REPORTS.

Author.	No. tubercular cases.	No. valvular lesions.	Per cent.	Mitral.			Aortic.			
				Insufficiency.	Stenosis.	Both.	Insufficiency.	Stenosis.	Both.	
Phipps' Institute, Philadelphia, 1904.	1,276	76	5.9	45	24	...	3	4	...	
L. Brown,* 1904. Saranac Lake.	600	5	0.8	4	1?	0	0	0	0	1 case mitral insufficiency with doubtful tuberculosis.
J. A. Burroughs,* Asheville, N. C.	4 987	321	6¼	...	...	...	...	...	...	Aortic lesions 32 mitral " 289
J. F. Russell,* Post-Graduate Disp., New York.	1,500	15	1.0	...	...	...	...	...	...	Individual lesions not recorded.
Carrington,* Fort Stanton, N.M.	329	22	6.7	19	1	1	1	1	1	Pulmonary stenosis 1.
E. S. Bullock,* Silver City, N. M.	1,000	20	2.0		...	...	...	...	...	Individual lesions not recorded.
K. von Ruck,* Asheville, N. C.	3,009	43	1.0	21	2	6	2	1	1	Aortic insufficiency complicated by mitral insufficiency 2, pulmon. stenosis 10.
Meisenburg.	4,649	53	1.14	34	0	5	5	2	1	Mitral and aortic insufficiency 2, pulmon. stenosis 4.
J. M. Anders,[35]	94	6	6⅜	4	2	0	0	0	0	
Milliken,†	00	3	5.0	2	1	0	0	0	0	
A. Abrams,†	800	21	2⅝	9	3	3	0	2	0	Pulmonary stenosis 1, unclassified 3.
E. Baldwin,†	1,200	9	¾	7	1	0	1	0	0	
Turban,[36]	408	8	1.9	5	1	0	0	1	1	
Fischer, Wallis,[32]	597	6	1.0	2	1	1	0	0	0	Pulmonary stenosis 2.
Planegg Sanitarium,‡ Munich.	812	8	0.9							
Basler Sanitarium,‡ Davos.	1,080	9	0.8							
Wald Sanitarium,‡ Zurich.	506	4	0.7							
Cotton,[33]	1,000	2	0.2							
A. Eyman,[19]	27,653	80	0.2							Individual lesions not given.
Roepke,[114]	300	3	1.1	3	0	0	0	0	0	

* Personal communication. † Quoted by Anders. ‡ Quoted by Fischer.

The records gathered from the Philadelphia Hospital showed a relatively larger number of aortic lesions than did those from the other institutions, a result which is easily explained by the fact that more of these cases were advanced in life. The patients at the Phipps Institute, on the other hand, were mostly young, their death with a few exceptions having been due to the last-named disease.

STATISTICS FROM AUTOPSIES UPON CASES OF PULMONARY TUBERCULOSIS.

Author.	No. autopsies.	No. valvular disease.	Per cent.	Mitral.			Aortic.			
				Insufficiency.	Stenosis.	Both.	Insufficiency.	Stenosis.	Both.	
Kidd,[37]	500	27	5.4	16	1	1	11	0	2	Tricuspid 2.
Carrington,*	38	8	21.0							
Cotton,[38]	503	55	7.0							
Saenger,[31]	469	3	0.64							
Williglk,[39]	1317	1	0.08							
Reissner,	152	0	0							
Chambers,[40]	566	0	0							
v. Kryger,	1100	10	0.9	3	1	...	4	...	1	Aortic and mitral insufficiency 1.
Otto,[43]	185	29	1.5	...	...	...	...	...	...	Endocardial thickening, especially mitral.
Fenwick,	1560	30	1.9	14	5	0	9	5	0	Endocardial thickening in 12 per ct., 13 acute lesions not definitely.
Norris,	1764	130	7.3	51	14	11	37	9	18	Tricuspid stenosis 2, tricuspid insufficiency 12, pulmonary insufficiency, 1.

If we investigate the frequency with which valvular disease of the heart is complicated by pulmonary tuberculosis we find a number of statistics the import of which lead to similar conclusions. Otto[43] has especially investigated the relation of sex in relation to the present question, and states that tuberculosis of the lungs is more often engrafted upon women suffering from valvular disease than is the case in men. The preponderence of mitral lesions is again evident in the following tabulation:

AUTOPSY STATISTICS IN CASES OF VALVULAR HEART DISEASE.

Author.	Autopsies on heart cases.	No. with pulmonary tuberculosis.	Mitral.			Aortic.			
			Insufficiency.	Stenosis.	Both.	Insufficiency.	Stenosis.	Both.	
Frommolt,	277	22	8	3	1	7	3	...	Aortic stenosis and tricuspid insufficiency 1.
Otto,	48 (in men).	0	22	2	2	4	1	0	Combined lesions, 17.
Otto,	63 (in women).	4	27	10	13	3	2	1	Combined lesions, 11.
Norris,	57	...	8	0	2	8	0	2	

* Personal communication.

CLINICAL REPORTS ON CASES OF VALVULAR HEART DISEASE.

Author.	No. heart cases.	No. pulmonary tuberculosis.	Per cent.	Mitral.			Aortic.			
				Insufficiency.	Stenosis.	Both.	Insufficiency.	Stenosis.	Both.	
Meisenburg,	760	53	7.0							
Eyman,	4138	69	1.7							
Germain See,	277	22	8.0							
Walsham,	91	3	...	...	91					
Schultze,	484	109	22.5	...	...	...	...	...	...	Mitral 4.76 %, aortic 15.4 %, tricuspid 12.8 %, pulmonary 81.3 %; had tuberculosis.
v. Kryger,	59	10	16.9	4	1	0	5	0	1	All ten healed tuberculosis.
Birch-Hirschfeld,	107	5	4.6	...	...	...	...	...	...	2 cases pulmonary stenosis; found 20.8 % tuberculous lesions in individuals without heart disease.
Gillespie,[108]	2368	49	2.06	14	9	6	7	...	3	Tricuspid, 1.

Unfortunately the majority of available statistics, including my own, which deal with the occurrence of recent endocarditis in pulmonary tuberculosis, give no information regarding the microscopic findings or bacteriological examinations. The frequency with which this condition is encountered is shown in the appended tabulation:

	Tuberculous autopsies.	Recent endocarditis.	Per cent.
Teissier	100	32	32.0
Schultze	6937	67	0.966
Osler[42]	216	12	5.5
Kidd	500	6	1.2
Norris	1764	16	0.9
Fenwick	1560	13	0.7
Otto	185	4	3.1
Dittrich[113]	403	1	0.24

Doubtless in the majority of the above cases the acute endocarditis was due to other causes than the tubercle bacillus. In one of Osler's cases fresh tubercles were found upon the mitral leaflet, but no tubercle bacilli could be demonstrated in the sections. Kidd and Councilman also failed to find them. Even when the bacilli can be demonstrated, it is perfectly possible that their presence was simply accidental, as a roughened endocardium would present a favorable ground for the lodgement of micro-organisms carried thence by the blood stream. Lancereaux,[57] Letulle,[58] Perroud,[59] Traube,[60] Fenwick,[61] and others have reported cases of tuberculous endocarditis, but inasmuch as bacteriological evidence is lacking their identity cannot be proved. Anders,[62] who has written an excellent article on the subject, states that these cases are often "associated with other forms of cardiac tuberculosis, especially the pericarditic."

Simple sclerotic endocarditis is met with very commonly in pulmonary tuberculosis, and is presumably due to the toxæmia which is present in the chronic variety of this disease. The researches of Auclair[63] have shown that the metabolic products of the tubercle bacillus possess sclerogenetic as well as necrogenetic properties, which would readily account for the endocardial thickening. Boinet and Romary's[64] experiments have proved that bacterial toxin, even in the absence of bacteria themselves, and without the addition of trauma, are capable of producing changes in the endocardium and aorta. "Ectasine," the vasodilatory substance which Bouchard has shown to be a constituent of the tuberculous toxin by producing vascular relaxation would favor diapedesis of the leukocytes, thus paving the way for sclerogenous processes.

Teissier has enunciated the belief that mitral stenosis is frequently produced by the prolonged action of the tuberculous toxin upon the endocardium, which in time results in a narrowing of the valvular orifice, and states that this form of valvular lesion exerts an inhibitory effect upon the pulmonary disease. If such an inhibition exists, it is more probably due to the increased resistance which the bodily tissues have acquired through the prolonged presence of the toxin in the system than to the mechanical action of the stenosis. Chartier[102] remarks that this sclerogenous tendency is not tuberculosis, but the index of immunity versus tuberculosis.

A tuberculous process may of course be engrafted upon a preexisting valvulitis of different etiology, or the condition may be reversed. Cardiac murmurs occur so frequently in tuberculosis, especially in its later stages, and true tuberculous endocarditis is so rarely encountered, that the condition is hardly ever diagnosticated during life, although this has been done in a few instances. Cases reported as such, in the absence of post-mortem substantiation, have absolutely no value. An interesting case has recently been reported by Debove;[65] an individual, aged thirty-four years, died in a cachectic condition, and at autopsy tubercle bacilli were found in the blood and in the mitral vegetations, no tuberculous lesions being encountered elsewhere. Teissier has classified the various forms of tuberculous endocarditis as follows:

Tuberculous Endocarditis (bacillary).

a. Granular, discrete or confluent.

b. Caseous.

c. Nodular (vegetative).

Endocardial Sclerosis (toxic).

a. Generalized.

b. Localized.

Heller,[45] Cornil,[46] and Kundrat[47] were among the first to describe tuberculous endocarditis, but the credit of the first definite and accurate report of this condition belongs to Tripier,[48] who, in a case

of miliary tuberculosis, found a small nodule on the anterior leaflet of the mitral valve which showed the characteristic cellular changes upon microscopic examination, as well as the tubercle bacillus itself. Some time afterward v. Leyden[21] reported four similar cases, in one of which the condition was diagnosticated antemortem. Lion,[67] Londe and Petit[66] demonstrated tubercle bacilli in the valvular endocardium, but derived negative results from inoculation experiments. Similar results were obtained by Etienne,[49] de Thiry,[50] Benda,[51] Poncet and Dor,[52] Ferrand and Rathery,[53] Michaelis and Blum,[54] were the first to succeed with inoculation by producing tuberculous endocarditis in rabbits; and finally Braillon and Jousset[56] demonstrated tubercle bacilli in the blood of a man dying of primary tuberculous endocarditis, the only other evidences of this infection having been a few pleural adhesions. Tuberculous endocarditis usually assumes a verrucose, but sometimes an ulcerative form. According to Benda, the majority of these cases have their origin in a miliary infection, which happens to become localized upon the valves, being in this respect analogous to the condition described by this author as tuberculous endangeitis. In searching through the records of the Philadelphia Hospital two cases were found which were designated as "tuberculous endocarditis;" small tubercles had been found upon the valves, but apparently no microscopic examination had been made.

Vaquez[68] reports a case with very slight pulmonary involvement which developed the signs of an acute mitral endocarditis with cardiac dilatation, the patient rapidly succumbing with evidences of œdema of the lungs. Post-mortem examination of the heart showed a recent marginal mitral endocarditis, in the verrucose structure of which tubercle bacilli were demonstrated. In Ferrand and Rathery's case primary tuberculosis of the spleen was complicated by endocarditis, tubercle bacilli being found in the heart clots and the valvular vegetations. The mode of infection in these cases, the valves themselves having few or no bloodvessels, is probably derived from the heart's blood; lymphogenous infection is of course also possible. The cardiac enfeeblement which occurs in the later stages of tuberculosis would favor the deposition of fibrin upon the endocardium, in which tubercle bacilli could be readily enmeshed. Some cases are due to direct extension of the process from a tuberculous myocarditis. It is much to be desired that microscopic examinations be made of all valvular abnormalities occurring in individuals who show tuberculous lesions in any part of the body.

The effect of valvular lesions upon the course and curability of pulmonary tuberculosis is an interesting one. Some authors, among whom Graham[55] may be mentioned, state that the presence of the former condition, especially when mitral insufficiency exists, and is accompanied by good compensation, exerts a favorable influence

upon the pulmonary disease. von Kryger's 1100 autopsies showed 59 cases of valvular lesions associated with a healed tuberculosis of the lungs. Among 1606 autopsies at the Philadelphia Hospital I found 145 cases of healed pulmonary tuberculosis, 73 of which were associated with abnormal hearts; 35 of these being valvular lesions, and 38 showing well-marked hypertrophy, in the majority of instances due to arteriosclerosis or nephritis. Of the former 27 affected the mitral, 25 the aortic, and 2 the tricuspid valves. Two cases were described as "healing tuberculosis," in one of which a double mitral lesion was present, in the other "chronic endocarditis of the mitral and aortic valves." It is necessary to state, however, that in many of the foregoing cases there was no positive evidence of impaired valve action; a number of them having been simply designated as "chronic endocarditis," "aortic sclerosis," etc. Aneurysm of the aorta was found eight times in 1764 tuberculous autopsies, in one instance it was associated with a healed process. It will be remembered that this is one of the conditions which Rokitansky believed to have an immunizing effect. Fuller[69] states that about 7 per cent. of all cases of aortic aneurysm show evidences of pulmonary tuberculosis; the Brompton Hospital reports show that 7 out of 24 cases of aneurysm were complicated by tuberculosis. Lebert's statistics show this condition in 6 per cent. of the cases. The question as to whether the heart lesion preceded or followed the pulmonary tuberculosis has in quite a large number of instances been carefully determined. In 11 out of 27 cases Kidd[37] found that the heart disease had been first established. Meisenburg[27] reported 49 cases in which a similar state of affairs had existed; in none of these, however, was mitral stenosis present. Duchamp[94] has reported a case of a girl who at the age of eight had chorea, with endocarditis, who suffered from valvular incompetency for years, finally dying at the age of twenty-two of pulmonary tuberculosis. Lannois[95] has recorded an instance in which an individual who had had four attacks of rheumatic fever which resulted in producing both mitral and aortic insufficiency, deve'oped and died of an acute tuberculosis of the lungs. Brousse and Duchamp[96] have noted the occurrence of pulmonary tuberculosis in a girl who had shown the symptoms and signs of mitral insufficiency for years. Otto,[43] after a careful study of the clinical and pathological records of Eichhorst's clinic, covering a period of eleven years, found the coincident presence of pulmonary tuberculosis and heart disease in 6.3 per cent. of the women, but failed to find any such instances among the men. She therefore concludes that the simultaneous occurrence of the two lesions is by no means incompatible, and that malnutrition of the cardiac muscle and insufficient compensatory hypertrophy are conditions which render a tubercular infection more readily possibly. Schultze[35] found antecedent cardiac disease 42 times in 109 cases of pulmonary

tuberculosis, and similar experiences might be quoted almost indefinitely.

When tubercle bacilli enter the blood stream, which they may do either through the pulmonary veins or by direct transmigration from a neighboring focus, they may gain a foothold upon some localized area of the intima, producing either superficial tubercles, infiltration, total occlusion of the vessel, or ulceration, in which case aneurysmal dilatation of the vessel may occur. The latter incidence has been observed in a canine case reported by Hektoen.[70] Cardiac thrombi are a common autopsy finding in pulmonary tuberculosis; Warthin[71] found them in 10 per cent. of his cases; the only case in which a microscopic examination of the clot was made revealed the presence in the basal layers of "epithelioidal tissue containing numerous giant cells, and showing a beginning caseation," red blood cells, fibrin, and tubercle bacilli were also demonstrated. The latter have been found in cardiac thrombi by Weichselbaum,[72] Klebs,[73] Birch-Hirschfeld,[74] Kotlar,[75] Chiari.[76]

Tuberculosis of the aorta occurred only once in the present series of cases. The anterior surface of the vessel underlying the pericardium showed two projecting caseous nodules about the size of a split pea, surrounded by an inflammatory zone, the primary seat of the infection having apparently been in the lungs.

Within the last year Simmitsky[77] has reported two instances of this condition, and collected eighteen from the literature, in which collection are included the cases which are incorporated in Blumer's[78] paper some years before. Tuberculosis of the aorta may arise in four ways: first, by the direct extension of a tuberculous process outside the vessel walls; second, and most commonly, by the deposition of tubercles upon the intima, in which process the other two vascular coats may be but are usually not involved; third, by the infection travelling through the vasa vasorum, the latter case being rather rare, as is shown by the infrequency with which the media has been found to be the seat of disease; fourth, by lymphatic infection, although this necessitates the assumption of an invasion in the opposite direction to the current. As has already been pointed out, the dislodgement of tuberculous thrombi may produce an endangeitis. In a case reported by Kamen,[79] a tuberculous gland which had become adherent to the aorta ruptured into that vessel; as a rule, however, the condition occurs as part of a general miliary invasion. Simmitsky's investigations showed two such cases occurring in 135 instances of the last-named process. From the evidence thus far obtained one is led to believe that arterial lesions such as atheroma or calcareous degeneration, while favoring the deposition of tubercles upon the intima, are by no means a requisite for their production.

Tuberculosis of the myocardium was mentioned by Laennec[111] in 1826; but the first case on record is that reported by Townsend[80]

in 1832. Since then the condition has been studied by numerous observers, among whom may be mentioned Saenger,[81] Pollak,[82] Valentin,[83] Mendez,[84] Labbé,[85] and Anders;[86] in the excellent paper of the latter will be found an extended bibliographical list of authors antedating 1902.

Myocardial tuberculosis manifests itself in four ways:

1. *Large Tubercles.* These may be single or may result from the conglomeration of smaller tuberculous foci. They vary from a small pea to a hen's egg in size. These nodules have a caseous centre and may very closely simulate gummata, a fact which has been attested by Virchow himself.

2. *Diffuse Tubercular Infiltration.* This, the rarest variety, is usually seen in those cases in which the myocardium has become involved as the result of direct extension from the pericardium, the muscular tissue being to a considerable degree destroyed.

3. *Miliary Tubercles.* In these cases the usual miliary tubercles are found underlying but, as a rule, not involving the endocardium, on account of which they are easily overlooked.

4. *Fibroid Tuberculous Myocarditis.* The existence of this form was for some time questioned inasmuch as Brehmer's[87] case was the only one on record. Since then, however, a similar case has been described by Gandy,[89] and a definite identity established. The pathological findings in these cases consist of diffuse infiltration of round cells and connective tissue. Microscopically, giant cells, caseous areas, but no tubercle bacilli have been demonstrated. This variety of myocarditis is presumably due to toxæmia, being comparable to tuberculous cirrhosis of the liver and similar to the muscular sclerosis found in the horse by Cadiot, Gilbert, and Roger,[88] as well as the muscular fibrosis of chronic tuberculosis described by Klippel.

Nearly half of the reported cases of tuberculous myocarditis occur in individuals under fifteen years of age, no especial predilection for sex having been noted. The majority of the cases seem to owe their origin to infection of the pericardium; the endocardium, on the other hand, does not often seem to share in the extension of the disease. The following table shows the frequency with which the condition has been encountered.

			Per cent.
Rokitansky	116	2	1.7
Louis	112	0	0
Willigk	1825	2	0.1
Valentin[83]	3203	7	0.21
Chambers	566	2	0.3
Sangali[90]	796	2	0.2
Fuchs[91]	285	1	0.4
Dittrich	403	1	0.28
Norris	1764	5	0.28

Stephani[92] has during the past year collected and tabulated most of the reported cases of large conglomerate heart tubercles

from the literature and found but 36. Localized areas of myocardial tuberculosis as an accompaniment of tuberculous pericarditis is quite a frequent autopsy finding, but large caseous masses are a considerable rarity. Kaufmann,[97] in his *Pathological Anatomy*, states that he has seen a tuberculous mass the size of a goose egg involving the wall of the right auricle.

The source of infection in myocardial tuberculosis, in the same manner as when the pericardium is thus involved, is usually from the bronchial or mediastinal glands. The frequency with which these structures are the seat of an active or latent tuberculosis has been pointed out in another paper.[93] Cabannes[98] has written an article upon tuberculosis of the auricles in which he calls attention to the enormous size of the tubercles which have been found infiltrating these structures; according to the last named author these cases owe their origin to infection from the adjacent lymphatic glands. Primary tuberculosis of the myocardium has been described by Demme,[99] Noel,[101] and Knopf, but the existence of such a condition has not been generally accredited. In 1764 tuberculous autopsies I was able to find tuberculous myocarditis six times. In one case small miliary tubercles were found scattered through the muscle fibres in a case of acute general infection; the other cases were associated with tuberculosis of the pericardium; none of the cases showed large caseous masses. Microscopic examinations of the cardiac muscle were recorded in 41 tuberculous cases at the Pennsylvania Hospital with the following results:

Normal muscle	14
Chronic interstitial myocarditis	10
Parenchymatous degeneration	9
Fatty degeneration	5
Brown atrophy	3

Cultures were made from the heart's blood in 21 cases of pulmonary tuberculosis, resulting as follows:

Sterile	14
Micrococcus lanceolatus	3
Staphylococcus pyogenes aureus	1
Streptococcus mucosus	1
Micrococcus citreus	1
Bacillus alkigenes	1

The foregoing results tend to substantiate the observations of clinical experience. In the wards of the Phipps Institute, where a considerable number of patients with advanced pulmonary tuberculosis are assembled, it has frequently been observed that after remaining in a stationary condition for a considerable length of time, five or six individuals will often die in rapid succession and without very evident cause, suggesting the fact that this sudden rise in the mortality rate has been due to an acute infection which had gone the rounds of the ward.

Tuberculous myocarditis may be closely simulated by gumma, carcinoma, and actinomycosis. The first of these is to be distinguished from tuberculosis by being more sharply circumscribed from the surrounding tissue, when microscopically examined, and also by being grayer in color. Carcinoma contains less moisture, and is more brittle. Actinomycosis may be impossible of differentiation, unless tubercle bacilli or hooklets are found.

CONCLUSIONS. 1. In view of the frequency with which tuberculosis of the lungs has been found to be associated with valvular heart disease, we are forced to conclude that the latter exerts, if any, but very slight influence upon the former, either as an inhibitive or curative influence, even if satisfactory compensation is maintained. On considering the relative frequency of valvular lesions in general, mitral stenosis does not seem to be less often coincident with tuberculous disease of the lungs than other varieties of heart lesion.

2. It is doubtful whether smallness of the heart predisposes to pulmonary tuberculosis of the lungs to a greater degree than is explainable by the general systemic underdevelopment and lack of resistance which such individuals often exhibit. It is a fact, however, that small hearts, either as the result of wasting or hypoplasia, are commonly found at tuberculous autopsies, while large hearts are not often encountered in uncomplicated cases.

3. Stenosis of the pulmonary orifice seems to favor the development of tuberculosis of the lungs. A very large proportion of these cases die of the latter disease.

4. Arterial and endocardial thickening is a common result of tuberculous intoxication, but it is doubtful whether this process attains a sufficient degree to produce valvular incompetency, as claimed by Teissier.

5. Tuberculous endocarditis and myocarditis, particularly the former, occur with considerable rarity, but pericarditis, especially the chronic forms, very frequently owe its existence to the presence of the tubercle bacillus.

6. Tuberculosis of the aorta is also a finding of considerable rarity; the condition may result in the formation of an aneurysm.

7. The cardiac muscle undergoes various forms of degeneration in pulmonary tuberculosis, fatty and fibroid changes being very common, a fact which explains the signal failure of digitalis and certain other heart stimulants to benefit these cases.

8. Uncomplicated cases of pulmonary tuberculosis often exhibit such striking differences in resistive power and frequently evince such a remarkable tendency toward recovery, even in seemingly hopeless cases, that we should accept only the most absolute evidence as a proof that either the coincidence of another pathological condition or the administration of a special remedy has conferred a benefit upon the patient.

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CONCERNING HÆMAGGLUTININS OF BACTERIAL ORIGIN AND THEIR RELATION TO HYALINE THROMBI AND LIVER NECROSES.*

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Elsewhere one of us[1] has described the hæmagglutinative power of various cytolytic immune sera and the relation of the red blood corpuscle thrombi (hyaline thrombi) resulting from the injection of such sera to focal hyaline necroses of the liver. The distinct character of the liver lesions thus produced and the fact that they could be explained only by the presence of agglutinated red blood corpuscle thrombi suggested the possibility that similar lesions occurring in various infectious diseases might be due to the development of hæmagglutinins of bacterial origin. In order to test this supposition we have attempted to demonstrate the presence of hæmagglutinins in filtrates of bacteria treated in various ways and by the injection of the same into animals to produce agglutinated red blood corpuscle thrombi and associated liver necroses.

It is not our intention to go into the general literature of these subjects, but merely to touch upon those points which relate to infectious conditions. The more important views concerning liver necroses may be found in the papers of Flexner,[2] Mallory,[3] Boxmeyer,[4] and Opie.[5] That the so-called hyaline thrombi may be composed of altered and fused red blood corpuscles, we consider to be definitely established. The recent studies of Flexner,[6] Boxmeyer and Pearce offer conclusive evidence of such origin, and support the earlier observations of Klebs[7] and Ziegler.[8] The occurrence of hyaline thrombi in connection with various infectious and toxic conditions has been emphasized by Welch,[9] who, in his summary of the literature mentions particularly infections with S. pyogenes aureus and B. choleræ suis, and offers a suggestion concerning their origin from red blood corpuscles. In a later discussion[10] of the subject he brings forth the hitherto unpublished observation of Fisher concerning the plugging of small vessels by agglutinated red cells, as the result of injecting typhoid bacilli, and calls attention to the evidence in favor of the interpretation of many of the hyaline thrombi

* This study has been conducted under a grant from the Rockefeller Institute for Medical Research.

as derived from fused red blood corpuscles. Other important observations are those of Flexner, who found similar thrombi in the intestine of typhoid fever, in bronchopneumonia, and in experimental diphtheria; and also of Boxmeyer who could distinguish, in the livers of rabbits dying of experimental hog cholera, between necroses due to endothelial cell thrombi and those due to agglutinated red blood corpuscle thrombi. The hyaline thrombi occurring in various intoxications due to either organic or inorganic poisons, and in toxic conditions of doubtful origin, as eclampsia, are undoubtedly of similar nature; but as they do not come within the scope of this paper, will not be further considered.

Of considerable historical interest, in connection with this question of the occurrence of red corpuscle thrombi in the course of infectious diseases are the observations of Hueter,[11] made in 1873. As the results of his studies, to which attention has recently been called by Welch,[10] Hueter came to the conclusion that clumping of red blood corpuscles causing permanent or transient occlusion of capillaries and small vessels ("globulöse Stase und Embolie") occurred not uncommonly in septic and other fevers. His theory that this phenomenon constituted the underlying basis of fever has never gained acceptance, but the observations are of interest in connection with our recently acquired knowledge of bacterial hæmagglutinins. v. Recklinghausen[12] considers this globular stasis of Hueter to be analogous to a condition found in the capillaries after transfusion of alien blood, and which he described as an "agglutination" of red blood cells.

In planning this investigation it was evident that as necroses of the liver are most frequently associated with infections by the bacillus of typhoid fever and the bacillus of hog cholera, the bulk of the work should be done with these organisms. In order, however, that no opportunity might be lost, the literature dealing with bacterial hæmolysins was examined in the hope of finding references to organisms which produced also hæmagglutinins. Of twenty-nine such investigations,[13] but six[14] refer to the production of hæmagglutinins by bacteria. Kraus and Ludwig found that bouillon cultures of S. pyogenes aureus and Vibro Paris had the power of agglutinating red blood corpuscles, *in vitro*, in from ten to twenty-four hours at room temperature. The mass which settled at the bottom of the tube was seen upon agitation to be composed of small clumps of red blood corpuscles which could not easily be disintegrated. The agglutinin they considered to be independent of the hæmolysin; but, on the other hand, they state that organisms which do not hæmolyze also do not agglutinate. Small amounts of the cultures caused agglutination without hæmolysis. Volk and Lipschütz, working with staphylolysin and vibriolysin, describe agglutination in connection with incomplete hæmolysis of rabbits' blood, but did not observe it with other bloods. Volk, as a result of his

observations, comes to the conclusion that agglutination is due not to a specific body, but to non-isotonicity of the fluid. Calamida states that no agglutination precedes the hæmolysis caused by bouillon cultures of the chicken-cholera bacillus. Flexner mentions agglutinins of low activity in filtrates of B. pyocyaneus, B. typhosus, and S. pyogenes aureus. Kayser, in his study of colilysin, observed a clumping of red cells in connection with incomplete hæmolysis, but not when complete solution occurred. Of greatest interest, however, and very suggestive, is the observation of Eisenberg,[15] who found the blood of an individual with a generalized pyocyaneus infection to be both autoagglutinative and isoagglutinative.

As the result of this survey it seemed advisable to utilize B. pyocyaneus and S. pyogenes aureus in addition to B. typhosus and B. choleræ suis; and these with B. dysenteriæ and S. pyogenes constituted the group of organisms finally selected for study.

METHODS. In previous attempts (Reed,[16] Flexner, Mallory and Boxmeyer) to produce liver necroses by the injections of micro-organisms, either the living culture grown in the ordinary way or its filtrate has been used. With the use of the former it has been difficult to distinguish between the direct action of the organism and the effect produced by its toxin; with the latter the action of intracellular toxins has been excluded. In our experiments the direct action of the micro-organisms has been eliminated by the use of filtered fluids, and an attempt has been made to obtain the intracellular constituents of the bacterial cells by the utilization of methods destined to cause its disintegration. Various writers have described methods by which the bacterial cell is destroyed and its receptors liberated. Of these methods we have tried, with certain modifications, the processes of autolysis described by Conradi,[17] Neisser[18] and Shiga, and Brieger and Mayer.[19] The various organisms have been grown for twenty-four to seventy-two hours on agar in large flat flasks having a surface of 20 x 8 cm. The growth on several flasks, usually three or four, has then been scraped off, subjected to 55° C. for forty-five minutes, and placed in tubes containing 0.85 per cent. salt solution at a temperature of 37.5° C. for two to three days. In some instances the fluid has stood for longer periods, varying from one to seven weeks. The fluid has then been filtered (Chamberland B. and F.) and injected intravenously into animals, after testing its agglutinative power *in vitro*. At various stages of the process suitable controls were made to demonstrate absence of contamination and the efficiency of the filters.

In addition to this method of growing the organism, an attempt was made also to stimulate the production of hæmagglutinin by previously growing the organisms in media containing red blood cells. This method was suggested by the theory of "bacteriogenic cytotoxins" advanced by Welch in his Huxley Lecture: "Certain

substances of the host of cellular origin, assimilated by the parasites through the possession of haptophore groups with the proper affinities, become anchored to receptors of the parasitic cell, which, if not too much damaged, is thereby stimulated to the overproduction of like receptors; these excessive receptors of the parasite, if cast off into the fluids or the cells of the host, then constitute intermediary bodies," etc. The writer further states "by a similar mechanism it is possible that parasites may be stimulated to the production also of antibodies other than cytotoxins, such as various agglutinins, precipitins, antienzymes—all adjusted against the host."

Assuming that if this hypothesis might apply to organisms growing in living cells or fluids, it might hold also for those grown on cells outside the body; typhoid and hog-cholera bacilli have been grown in various blood preparations. These include both defibrinated and washed blood added in various proportions to salt solution and fresh sterile rabbits' organs. The period of growth in the various blood mixtures varied from twenty-four to seventy-two hours; in some instances inoculations into fresh blood solutions or upon fresh organs being made on each of three successive days. The sterile organs were prepared according to the technique described by Flexner.[20] By these various methods it was hoped that the organism would be stimulated to produce agglutinins, and that this power would be retained during the subsequent growth on agar, giving in the finished autolyzed product a fluid of appreciably augmented agglutinating power. Observations supporting this theory have been made by Marmorek and by Simon, who found that streptococci grown in media composed of leukocytes alone, or with bouillon added, secrete a toxin of considerable power. Simon[21] believes that the streptococcus in order to secrete toxin must meet a certain resistance to its development, and that this resistance is furnished by something in the leukocytes. This explanation, put in the terms of Ehrlich, corresponds to Welch's hypothesis. Our attempts to produce free agglutinin receptors by growing the organisms in blood we consider analogous to Simon's method of producing toxin by growth in leukocytes.*

Another method employed was the growth of an organism in heated rabbit serum. This was suggested by the observation of Besredka[22] that the streptococcus produces an hæmolysin when thus grown.

RESULTS. The tests for agglutination were made by adding nine parts of the various filtrates to one part of blood. Obser-

* Another point in favor of this theory of bacteriogenic antibodies is the observation of Theobald Smith (verbal communication) that recently isolated cultures of the hog-cholera bacillus have a greater power to produce liver necroses than have old cultures. Accepting Boxmeyer's work on the relation of agglutinative red blood corpuscle thrombi to such lesions the explanation naturally suggested is that residence in the animal has stimulated the power of the bacillus to produce agglutinin.

vations were made at room temperature and at 37.5° C. at varying periods up to twenty-four hours. The clumping of red blood corpuscles by bacterial hæmagglutinins is of slight degree as compared with that produced by various cytolytic immune sera. The powerful agglutination of the latter is never seen, and for this reason more careful comparisons with controls is necessary in order to detect slight differences in reaction. This feeble activity renders it difficult to make definite statements concerning some of the organisms studied. While all (B. typhosus, B. choleræ suis, B. pyocyaneus, B. dysenteriæ, S. pyogenes aureus, and S. pyogenes) in the majority of tests *in vitro* showed a slight agglutination as compared with controls, the effect of filtrates of B. dysenteriæ, B. choleræ suis, and B. pyocyaneus was so slight as to be considered doubtful. With other organisms the agglutination was more evident, being most distinct with filtrates of S. pyogenes. Upon microscopic examination (hanging drop) the clumping caused by the streptococcus was always in the form of massive, more or less branching, rouleaux; while with all other cultures an irregular agglutination of a small number of corpuscles was seen. The agglutination due to the streptococcus could be seen after fifteen to twenty minutes as the corpuscles settled; while with the other organisms it could be seen only upon agitation after a considerable period of time. More definite results were obtained with rabbits' blood than with dogs' blood.

Of unusual interest and very suggestive are the agglutination tests with filtrates of typhoid bacilli previously grown in blood suspensions and on fresh sterile organs; though carried out in but a small number of tests they appear to be confirmatory of Welch's hypothesis mentioned above. These filtrates, especially those of bacilli grown on sterile organs, exhibit an appreciably greater power of agglutination than the filtrates of organisms grown on agar only.

While no effort was made to study especially bacterial hæmolysins, it is of interest that the autolytic products of bacteria as here prepared have never caused hæmolysis. This result is in harmony with the observations of Jordan,[23] Williamson,[24] and others, who hold that the hæmolysis produced by some bacterial filtrates (B. typhosus, B. pyocyaneus) is to be explained by the presence of an alkali elaborated in the growth of the organism. The filtrates used in our tests have all been faintly acid to phenolphthalein.

The animals selected for the injection experiments were dogs and rabbits, the former receiving 5 to 20 c.c. (dose, 1:1514 to 1:235) of the filtrates in either the saphenous or mesenteric vein; the latter 1 to 20 c.c. (dose, 1:1790 to 1:64) in either mesenteric or marginal ear vein. In all, twenty-nine injections have been made; in no instance did death occur as the immediate result of the injection. Necroses of the liver occurred in ten of the animals. Two of these we have thought best to exclude, because of associated coccidiosis,

although the necroses appeared to be entirely independent of the parasitic invasion; another has been excluded because of the chronic character of the lesion. The remaining seven cases exhibited typical necroses, two occurring in dogs and five in rabbits. These lesions followed the injection of filtrates of the typhoid bacillus in three cases, of the hog-cholera bacillus in three cases, and of the dysentery bacillus in one case. Filtrates of the B. pyocyaneus, S. pyogenes aureus, and S. pyogenes did not cause necroses. These necroses are not always visible to the naked eye, but when seen macroscopically they appear as miliary points, or occasionally as round or oval areas or linear streaks of grayish color and distinctly separated from the normal liver tissue. They are very few in number compared to those produced by the agglutinins of cytolytic immune sera, and are usually limited to the superficial portions of the liver lobes. Portions of the liver in contact with other lobes or adjacent organs are more frequently involved than the free surfaces. Histologically, the liver cells exhibit a hyaline necrosis, the nuclei being entirely destroyed or evident merely as faint rings; fragmented or pyknotic nuclei were seldom seen. In many of these areas the vessels are filled with red blood corpuscles, more or less altered and fused, and suggestive of hyaline thrombi. This condition, however, is not constant, and is not so evident as in the necrotic lesions produced by cytolytic immune sera. On the other hand, larger vessels, especially the smaller branches of the portal vein, contain typical agglutinative red corpuscle thrombi more or less completely occluding the vessel. Similar thrombi of small vessels have been seen in other organs, as the kidney, spleen, and lymph nodes, but without definitely associated lesions. Other thrombi, as those composed of endothelial cells, fibrin, etc., have not been seen in the liver.

Fatty changes in the liver and kidney, intense congestion of the spleen and lymph nodes, and a proliferation of the endothelial cells of the lymph sinuses have been found not infrequently after the injection of typhoid and hog-cholera filtrates. A relation between these lesions and the injected fluids cannot, however, be readily demonstrated; the proliferation of endothelial cells, especially, is not infrequent in apparently normal animals. That some injury to the kidney is brought about is indicated by the appearance of albumin in the urine after the injection of filtrates of B. typhosus and B. dysenteriæ.

The results of the injection of filtrates of typhoid and hog-cholera bacilli grown upon blood media, while very suggestive, are not conclusive, owing to the small number of observations. But six filtrates so grown were injected. Filtrates of the typhoid bacillus grown in blood suspensions, while possessing an increased agglutinating power *in vitro*, did not cause necroses upon injection; on the other hand, two different filtrates of the same culture grown for several

days on sterile rabbits' organs caused the most extensive lesions observed in the course of this investigation. The bacillus of hog-cholera grown in blood suspensions caused, in one instance, lesions in the liver. The attempt to produce necroses with such filtrates has therefore been successful in three of six experiments, while with filtrates of the same organism grown on plain agar, necroses resulted in three of twelve attempts. These results are suggestive in connection with the increased agglutinating power observed *in vitro*, but the small number of experiments does not warrant definite conclusions.

Filtrates of B. typhosus grown in heated rabbit serum produced no lesions upon injection into rabbits.

CONCLUSIONS. The filtered autolyzed products of a number of bacteria possess hæmagglutinins of low activity, the formation of which may be stimulated by previously growing the micro-organisms on media containing fresh red blood cells. The injection of these filtrates into dogs and rabbits is followed in some instances by the occurrence of liver necroses with associated fused red blood corpuscle thrombi; like thrombi may occur in other organs. These thrombi are similar in structure to those generally described as hyaline thrombi. The demonstration of agglutination *in vitro* and the association of the fused red cells with the liver lesions suggest a relation of the agglutinin to the lesions. This relation, however, cannot be considered as proven, for it is impossible to exclude the effect of toxins acting directly upon the liver cells; on the other hand, the similarity of the lesion to the very definite necroses caused by the powerful agglutinin of cytolytic immune sera strongly supports the possibility of such a relation.

The results observed by us are in accord with the slight potency of the agglutinin obtained. It is probable that methods which cause a more complete disintegration of the bacterial cells, as those employed by Vaughan,[25] and by MacFadyan and Rowland,[26] would yield an agglutinin as powerful, comparatively, as the toxins so derived, and capable of producing lesions more analogous to those caused by the agglutinins of cytolytic immune sera.

We present this communication, therefore, not as an attempt to prove that all hyaline thrombi are composed of fused red blood corpuscles or that all liver necroses are caused by such thrombi, but rather to indicate the evidence in favor of the view that these lesions, in some instances, may be due to bacterial hæmagglutinins.

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I. REPORT OF AN ANOMALOUS LATERAL SINUS. II. REPORT OF A CASE OF THROMBOSIS OF THE LATERAL SINUS.

By Barton H. Potts, M.D.,

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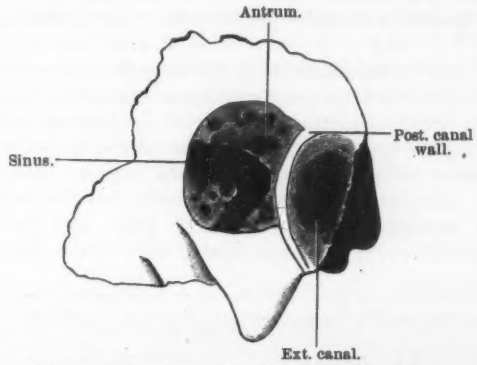
The first case is put on record because of the anatomical anomaly presented in the course of the lateral and sigmoid sinus. The patient was admitted to St. Mary's Hospital in an extremely low condition, and operated upon for cerebral abscess, but the condition grew steadily worse, and the patient died twelve hours after operation. No autopsy was permitted, and consequently a full description of the anomaly cannot be given. The accompanying illustration will show the course taken by the sinus. It lay immediately beneath

the external table and passed *through* the mastoid cells, being surrounded an all sides by pus, granulations, and mastoid cells. It looked exactly like a large tube passing through the mastoid space.

The horizontal portion crossed the mastoid space entirely, being separated from the external canal by a layer of bone not more than



Case I., showing passage of sinus across mastoid space.

3 mm. in thickness, and then made a sharp bend down and backward. It passed just below and external to the antrum instead of being on a level with it. It is to be much regretted that no autopsy was permitted, as it would have been very interesting to follow the complete course of the vessel.

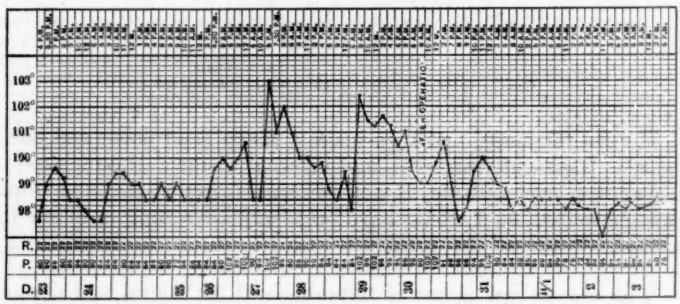
The second case is one of thrombosis of the lateral and sigmoid sinus. Mrs. K. S., aged twenty-three years, had most of the diseases of childhood, except scarlet fever. When a child she frequently had earache, but there is no definite history of a discharge. Present trouble began in October, 1903, when she complained of pain all over the head, tinnitus, vertigo, anorexia, and discharge from the right ear. The patient received careful treatment for her condition, but temporary relief only was obtained, and she was sent to St. Mary's Hospital by her physician, Dr. H. L. Picard.

Upon admission the pain was referred to the occiput, the mastoid, and the region behind the angle of the jaw. There was œdema over the mastoid and occiput, with doubtful tenderness along the jugular. The tympanic membrane was red and bulging, and the canal wall red and sagging. The presence of purulent mastoiditis was diagnosed, but, owing to the symptoms, the possibility of sinus thrombosis was considered, and it was decided to delay and keep the patient under close observation. The accompanying chart will show the characteristic temperature. Free paracentesis and incision of the canal wall, hot douching, and dry heat externally,

with calomel internally, was the treatment given and under which the pain was somewhat lessened.

On the fourth day after admission there was a sharp rise in the temperature, but close questioning failed to elicit history of a chill. The temperature fell gradually during the ensuing thirty-six hours, when there was another sharp rise of four degrees, and the patient said she noticed a clammy perspiration. Immediate operation was advised.

The usual tympanomastoid exenteration was done first; the sigmoid sinus was found uncovered and contained a firm clot. The bone was removed in the direction of the jugular bulb and backward along the lateral sinus, the latter also being filled with a clot. It was then deemed best to ligate the jugular vein before going farther. The vein was found to be soft, but the walls above the point of entrance of the facial were gray, and showed signs of clot formation. The vein was ligated about 3 cm. below and 3 cm.



above the facial, the latter was ligated and cut, and the jugular vein excised. The sinus wall was freely incised and a Randall sinus curette passed down toward the jugular bulb and backward through the lateral sinus for about 5 cm. until a free flow was obtained, as much of the clot as possible being removed. At first there was a considerable quantity of an offensive, reddish-brown fluid, and the flow was allowed to continue until the normal dark-blue blood appeared.

The neck wound was closed throughout with interrupted sutures, and the usual sterile dressings applied. On the fifth day following the operation the first dressing showed the neck wound healed by first intention, and the mastoid condition doing well. Convalescence was without complication of any kind, and healing has been perfect.

In most cases given, the œdema over the occiput, tenderness behind the angle of the jaw and over the jugular, operation might have been indicated by the first rise of temperature; but as this was coincident with marked constipation and the temperature fell

following an enema, and as no history of a chill could be obtained, it was thought best to wait.

The features of this and other cases of suspected sinus involvement would seem to clearly indicate that by far the best method of procedure is to open the mastoid early and uncover and carefully examine the sinus, for undoubtedly every hour counts in these cases. This patient, being under observation, was operated upon early enough to protect her from fatal infection; but in some of our cases that are not seen until the advanced stage of infection is reached, delay in intervention could unquestionably be serious or even fatal. In these cases the jugular vein plays a most important part, and decidedly the safest course would seem to be either to tie off the vein or excise as much of the vessel as its condition indicates.

A CASE OF GLIOMA IN THE SELLA TURCICA.[1]

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AND
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(From the Pathological Laboratory of the Boston City Hospital.)

Following is a case of new-growth in the pituitary region peculiar in producing an intercellular substance which stains like neuroglia. The tumor grew in all directions and notably forward and downward, with partial destruction of the gland and perforation into the sphenoidal sinus. Death occurred six years after onset of symptoms. There were symptoms of heightened intracranial tension, impairment of vision, an unusual kind of ("ear-to-ear") headache, and rhinitis. There was no acromegaly.

Clinical History. Mrs. ——, aged forty-eight years, family history good, previous health good.

History of present illness: Early in 1897 patient noticed slight impairment of vision. In July, 1898, the visual defect grew worse, and slight headaches developed. Dr. Knapp then examined her eyes, with results as follows: Right eye counts fingers eccentrically at 30°; left eye 20/40, with + 1 D. glass 20/30; ophthalmoscope shows right optic atrophy; no other intraocular disease. A second examination by Knapp in April, 1899, showed that right eye could see only movements of the hands; left eye with + 1 D. glass 20/30; there was complete bilateral temporal hemianopsia, and the nasal field

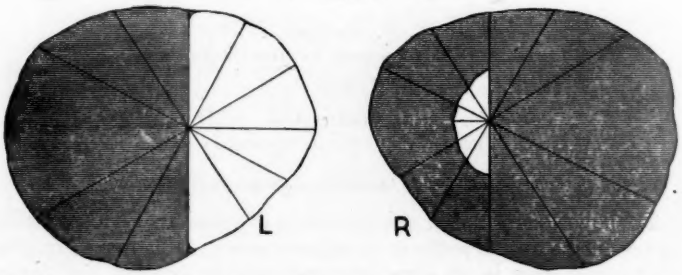
[1] Presented at the Fourth Annual Meeting of the American Association of Pathologists and Bacteriologists, New York City, April 2, 1904.

of right eye was much contracted, extending only 20 degrees toward the nasal side.

In August, 1899, there occurred an attack of coma ushered in by violent headache and nausea. With slight remissions, the attack lasted several days. There were no convulsions. Following this illness mercury inunction and potassium iodide were used, and the patient regained the degree of health possessed before the attack. During the winter (1899-1900) headaches became more frequent; they were often frontal in location, but frequently seemed to transfix the head, passing from ear to ear. Rhinitis developed, and with every exacerbation of the nasal congestion the headache became worse. There was some unsteadiness of gait.

In August, 1900, a briefer attack of coma occurred similar to that of 1899. In January, 1901, a third attack. One of us (F. H. H.) saw the patient in this attack. There was absolute coma, flushed face, slow, full pulse, fever, strabismus. There was and

FIG. 1.



Visual fields, showing bilateral temporal hemianopsia (from the notes of Dr. Herman Knapp two years after the onset of symptoms).

had been no sign of nephritis, neither was there paralysis at any time (except the ophthalmoplegia). There were no convulsions. The attack lasted about one week, during three days of which the patient was comatose.

A fair measure of health was regained after this attack, and maintained for two years. During this time the patient was fairly active, walking on the street daily, though with unsteady gait. There were occasional headaches. On two or three occasions there were transient seizures of violent headache and nausea, but without coma. The visual defect progressed until the right eye was totally blind and vision very defective in left.

In April, 1903, a final attack similar to former ones occurred and terminated in death.

(Dr. E. E. Mather, of Williamstown, physician to the patient, has kindly given us many of the clinical data. Notes of the ophthalmic findings have been kindly furnished by Dr. Hermann

Knapp, of New York. A part of the neurological account is due to Dr. M. Allen Starr, of New York, who saw the patient at various times during her disease.)

Clinical Summary. Symptoms at intervals during six years. Progressive impairment of vision. Frontal and ear-to-ear headache, more severe in attacks of rhinitis. Various seizures with headache and nausea. Attacks of coma forty-four, thirty-two, and twenty-seven months before death. Death in a fourth attack.

GROSS FINDINGS. *Necropsy.* Performed twenty hours postmortem. The cranium only was opened.

FIG. 2.

Ventral aspect of brain, showing tumor in interpeduncular space.

Body well nourished. Physiognomy normal. Calvarium of normal thickness. Pial vessels much engorged. No increase of arachnoid fluid. On raising frontal lobes a mass is seen in the neighborhood of optic chiasm, firmly adherent in places to sella turcica. Floor of sella thinned and broken through in places, opening into the sphenoidal sinuses, which contain pus. From below a conspicuous dark-brown mass is seen to occupy the interpeduncular space and to extend from the pons forward beyond the position of the optic chiasm. (Fig. 2.) The tumor hides all parts of the visual path except the extremity of the divided left optic nerve. Projecting from the tumor anteriorly, dorsally, and laterally into the right frontal lobe is a cyst of hazelnut-size containing a clear blood-

tinged fluid. A mesial section of the brain (Fig. 3) shows that the tumor lies anterior to the corpora albicantia, occupying the position of the pituitary body. The floor of the third ventricle is stretched over the dorsal surface of the tumor, and is melted down in part, so that the tumor projects into the third ventricle, encroaching to some extent upon the anterior portion of cavity. The tumor projects dorsally through cerebral substance into the lateral ventricle. The lateral ventricles are somewhat dilated.

The chiasm and the right optic nerve are totally destroyed. The tumor itself is thinly encapsulated and shells out easily from its bed of cerebral substance, and is of a spongy consistence anteriorly, more compact posteriorly. The spaces of the spongy tissue are filled with cruor clots.

Summary of Gross Findings. Single, compact, in places spongy or hemorrhagic tumor, filling interpeduncular space, producing atrophy of floor of sella turcica, encroaching upon lateral and third ventricles, and effecting atrophy and complete destruction of optic chiasm and right optic nerve, with partial destruction of optic tracts.

FIG. 3.

Mesial aspect of brain.

FINER ANATOMY. Endeavor was made to get at the duration of the process by tracing out roughly the degenerations in the optic apparatus. More evidence was obtained from the tissues of the tumor itself upon the crucial point of the relative age of its different parts.

The microscopic findings follow:

1. The cortex in many places, though not everywhere, exhibits slight neuroglia changes, consisting in a moderate increase of the large neuroglia cells of the subpial layer and an increase (or increased staining capacity) in the fibrillæ in the outermost lamina. We should like to interpret these changes as a response to the universal pressure and consequent flattening which attend new-growth or other swelling in intracranial tissues. Sections from the orbital cortex adjacent to the tumor show the thickest fibrillæ, which are

arranged as a rule tangentially. In general there are more fibrillæ in the sulci than over the tops of the gyri. There is some evidence for maintaining that there are more fibrillæ (without notable increase of cells of origin) opposite the vessels and especially opposite the larger arteries (compare fibrous increase in supra-arterial epicardial nodules). The method of demonstration here used was the phosphotungstic-acid-hæmatein method after formalin fixation and mordanting with picric acid and ammonium bichromate (Mallory).

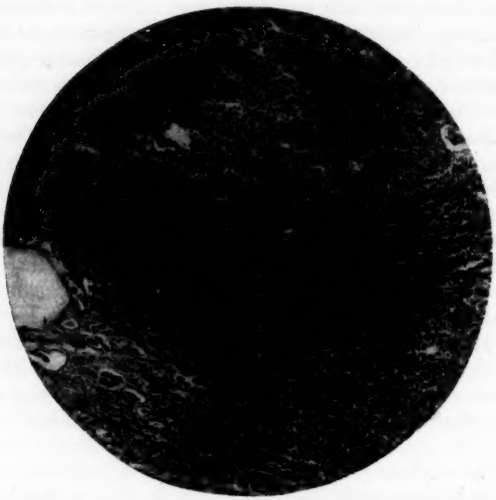
2. Work with the Nissl method (paraffin sections of formalin-fixed material) was negative or unsatisfactory. The adventitial spaces about the smaller vessels are free from exudative cells. Many of the isolated glia cells and some of the satellite cells show numerous coarse grayish-green pigment granules in limited masses serving very well to mark out the glia cell bodies which are not otherwise in evidence. Similar appearances are sometimes shown in Zenker-fixed material of various origin and without other lesion. Many of the nerve cells are moderately pigmented. The nerve-cell picture is unsatisfactory. Many of the nuclei are swollen; some show foldings of the nuclear membrane. The cell layers are demonstrable. The medullary glia shows an orderly arrangement of nuclei.

3. Unmistakable early degeneration is demonstrable by the Marchi method in the left optic nerve (central bundles show the most distinct blackening), in the left lateral geniculate body (dense bundles of degenerate fibres intercalated with normal bundles), in the left anterior quadrigeminal body (stratum zonale shows marked change, many of the sagittal fibres of the nucleus are blackened), and in the lateral geniculate and anterior quadrigeminal bodies on the right (diffuse changes).

Longitudinal sections of the left optic nerve stained by the Weigert method for myelin show almost total loss of staining capacity except in a central core (probably attacked last, as shown by the Marchi method). The lateral geniculate bodies and the anterior quadrigeminal bodies stain well by Weigert; probably all the fibres of the stratum zonale and most of the fibres of the nucleus retain the stain. A small area of undoubted degeneration of some standing was made out by the Weigert method in the left pulvinar; but this was not further traced.

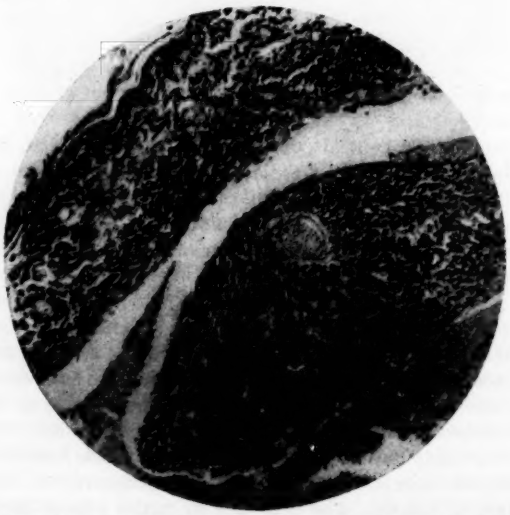
4. Microscopic examination of various portions of the tumor showed, first, some anterior pituitary substance; second, neoplastic tissue adjacent to and compressing the glandular substance. (Fig. 4.) The new formation showed an almost homogeneous structure except in amount of fibrillary intercellular substance. (Fig. 5.) The mass contains numerous well-developed vessels besides numerous thin-walled vessels, many of which have ruptured to form fairly wide lacunæ of blood. The cells are in many places so grouped about the vessels as to suggest the appearance of certain sarcomata of vascular origin.

FIG. 4.



Section showing strands of gland substance of anterior lobe of hypophysis compressed by the tumor. The gland contains numerous masses of colloid. The cytoplasm of the chromophile cells of the gland stains deeply with phosphotungstic-acid-hæmatein. (Mallory.)

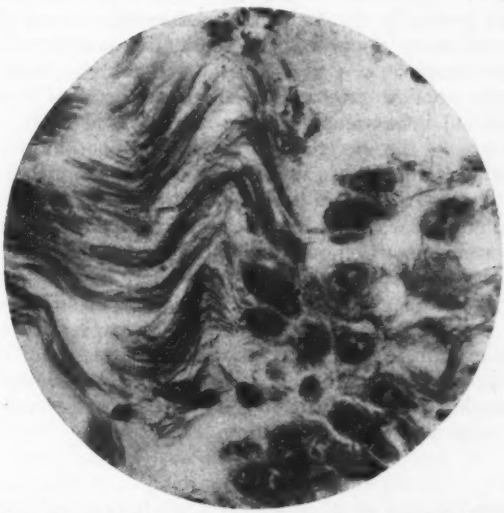
FIG. 5.



Low power view of tumor, showing trabeculæ of cells separated by a space containing blood and coagulated serum. The lower band of cells shows a striate or wavy structure due to the included fibrillæ. Section stained with Mallory's phosphotungstic acid-hæmatein (formol fixation, mordanting with picric acid and ammonium bichromate).

Owing to poor fixation or on some other ground it seemed impossible to prove the tumor a sarcoma by demonstrating an intercellular substance responding to the aniline-blue stain (Mallory). Attention was therefore drawn to a very few scattered fibrillæ taking the acid fuchsin in the aniline-blue method. With a view to making out the nature of these fibrillæ, pieces of the mass from a part adjacent to the bone were mordanted by the picric acid and ammonium bichromate process and stained by phosphotungstic acid hæmatein. By this method numerous bundles of parallel fibrillæ standing in the characteristic cage-like relation to the cells are demonstrable in the inferior peripheral layer of the tumor. (Fig. 6.) These

FIG 6.



High power view of tumor, showing bands of smooth, fairly coarse, parallel fibrillæ, bent about characteristically at acute angles. Field and staining method same as in Fig. 5.

fibrillæ are in places shown adjacent to the connective tissue which invests the older vessels, and can here be shown to differ in form as well as in staining reaction from the connective-tissue fibrillæ. The fibrillæ are demonstrable in fewer and fewer numbers as one advances toward the core of the tumor; but, whether they are not yet developed or for some reason do not stain, it is not possible to say. The fibrillæ of the peripheral zone can be demonstrated by phosphotungstic acid hæmatein alone (without the preliminary mordanting process) and also by Weigert's method for neuroglia fibrillæ.

The cells are rather large and of an oval or irregularly polygonal shape. The cells of the non-fibrillary core of the mass never show

processes and rarely reentrant angles; but the cells about which the fibrillæ are disposed are often supplied with numerous processes to which fibrillæ may sometimes be seen in close apposition. But few mitoses are demonstrable. There are, however, numerous cells with several nuclei, as a rule centrally set. No ependymal dots have been as yet discovered in the tumor.

(The microscopic examination was carried out in the pathological laboratory of the Boston City Hospital during the service of Dr. F. B. Mallory, to whom we are indebted for supervision of the work.)

REMARKS. The report may be summed up as follows:

A new-growth at the base of the cranium gives rise to somewhat characteristic symptoms ending in death after six years. The tumor has gradually filled the interpeduncular space, giving rise in the lower optic apparatus to certain degenerations, a part of which are complete, a part still in process. The brain at large shows little reaction save a subpial gliosis, perhaps incidental to the heightened intracranial tension.

The nature of the growth is in question. The oldest portion of the tumor (judging by the development of the fibrillæ) is in the locus of the posterior lobe of the pituitary gland, which lobe normally contains neuroglia cells developing fibrillæ. The rest of the tumor contains few demonstrable fibrillæ, and could scarcely be differentiated from a sarcoma. It is probably justifiable to classify the case as one of glioma developing in the posterior lobe of the pituitary body. We are not acquainted with previously reported cases of such tumors. Definite proof of the existence of this tumor type can only be brought when some fortunate case shall be dissected showing such a growth in the midst of, or patently growing from, an otherwise normal pituitary body.

A CASE OF DIABETIC GLYCOSURIA WITH INTERCURRENT ICTERUS AND NON-MEDICAMENTAL HÆMATOPORPHYRINURIA.[1]

BY HEINRICH STERN, M.D.,
OF NEW YORK.

DR. R. L., aged sixty-eight years, a retired clergyman, was seen by me in consultation with Dr. Savage on April 2, 1904. The present physician was first consulted in January of this year on the occasion of a slight accident for which local treatment afforded relief. Some weeks afterward a condition bordering on coma

[1] Read at the Meeting of the American Urological Association, Atlantic City, June 8, 1904.

set in. According to the description furnished by the attending physician and the members of his household, the attack was more in the nature of a stupor; Cheyne-Stokes respiration had not been noticed, and the patient defecated and urinated voluntarily. When out of the stupor, however, he could not remember anything at all about it. The condition was looked upon as diabetic in character, as he had been affected with more or less pronounced symptoms of diabetes for the past three or four years. Examinations of the urine made by patient's physician between January and April occasionally showed the occurrence of small amounts of glucose. Other abnormal urinary constituents besides albumin, which was never found, were not looked for. Microscopic examination was not deemed necessary.

In the beginning of March the patient developed icterus. The condition was very pronounced and was accompanied by several attacks, or periods, of chills. Temperature elevation had not occurred, but a subnormal temperature was noted on different occasions. The stools during the icteric period were clay-colored, the urine exhibited the features of the icteric state. The medication was symptomatic, no hypnotics of any kind were prescribed. (Sulphonal, trional, and tetronal were never administered.) Examination by me on April 2d revealed a dilated heart, slight pericardial friction, no valvular disease, normal rhythm, very weak impulse. The lunge were apparently normal. Stomach was slightly dilated, no hardness or structural alteration perceivable. The spleen was normal as to size. Colon and other parts of the intestines were slightly inflated, but fecal accumulations were not present. The liver extended about 3 cm. below the costal arch, the gall-bladder was enlarged and freely palpable. The parts adjacent to the liver were hard and caused pain on deep palpation; nodules could not be distinguished. Adhesions of metastatic processes were not detected. Kidneys could not be palpated. The various reflexes, though diminished, were present. The icterus could not be accounted for specifically; a provisional diagnosis of hepatic cirrhosis was entertained.

The patient complained of excessive weakness in spite of tonic medication. He had been on a light diet, including some cereals, which caused occasional intestinal disorders. The icteric condition was very pronounced and uniform. Examination of the urine exhibited the following facts:

Amount for twenty-four hours 850 c.c.; color very deep red; transparency slightly impaired; odor normal; reaction acid, 0.22°; specific gravity, 1023.5; salts of hydrochloric, sulphuric, and phosphoric acids about normal; salts of oxalic acid somewhat increased; carbamide, 17.85 grams; uric acid, traces; xanthine bodies, traces; creatin somewhat increased; hippuric acid, traces; urobilin, very large amounts; uroxanthin, traces; serum albumin, traces; biliary

acids and fatty matters absent; glucose, glycuronic acid compounds, alcaptonic acids, acetone, and diacetic acid absent. The microscopic examination did not reveal any excessive amounts of normal or any abnormal histologic elements.

The very outspoken dark-red color of the urine and the very large amount of biliary pigment led me to suspect the presence of some other specific coloring substance. Accordingly, the presence of hæmatoporphyrin was looked for. The urobilin, extracted from the urine by a modification of Garrod and Hopkins' process, was treated by the method devised by Saillet. A portion of the acid-ethereal extract was shaken with water. The water takes up the urobilin, but not the hæmatoporphyrin. Another portion of the acid-ethereal pigmentary extract was agitated with 5 per cent. hydrochloric acid. The latter takes up both coloring substances. After separation ammonia was added to the dilute acid; this was reacidulated with acetic acid and shaken with sulphuric ether. By this process the hæmatoporphyrin is extracted, while the urobilin remains behind. The hæmatoporphyrin obtained by the two methods was identified by spectroscopical examination. The examination on the days following after April 2d were made by the first method above described, by dissolving out the urobilin with water.

The presence of hæmatoporphyrin was found for fifteen days longer; daily examinations of the urine were made until March 20th. The amount of hæmatoporphyrin, though, gradually decreased until on the sixteenth day its presence could not be demonstrated any longer. The urobilin, however, continued to be excreted in very large amounts. In none of the specimens of urine examined until April 20th could glucose be demonstrated.

On May 14th I made a second examination of the patient. The icteric condition had greatly subsided, but was still of quite a pronounced degree, the patient, whose diet since April 2d had consisted mainly of milk and milk preparations, had experienced less trouble with his intestines, but felt very weak, and was extremely emaciated, his present weight being 132.5 pounds; two years ago he had weighed 210 pounds. I must mention that the patient's height is over six feet. The urine on this day exhibited no hæmatoporphyrin, but the amount of urobilin was still very large. Glucose was found for the first time on that day, and this to the amount of 7.5 per cent., which, the twenty-four hours' output of urine being 1400 c.c., amounted to 105 grams per day. The patient was put on a very rigid antidiabetic regimen, with the result that on May 21st his urine was entirely free from sugar and he felt himself much stronger. The ferric chloride reaction did not ensue on either occasion. Acetone could also not be demonstrated.

This case is of interest from two points: first, on account of the non-medicamental production of hæmatoporphyrin; and, second,

on account of the synchronous, respectively intercurrent supervention of the three symptomatic manifestations: icterus, hæmatoporphyrinuria and diabetic glycosuria.

Hæmatoporphyrin occurs in small amounts in normal urine and contributes toward its normal color. Its presence in large amounts is always a more or less abnormal phenomenon. Most cases of abnormal hæmatoporphyrinuria have occurred after the administration of sulphonal, trional, and tetronal. Excessive hæmatoporphyrin output is almost a constant symptom in chronic lead intoxication. Abnormal hæmatoporphyrinuria has been found in a case of Graves' disease, one case of hereditary syphilis, one of gastric ulcer with hæmatemesis, and in a few other diseases. In all these diseases its occurrence was accidental, it having been in no relationship with the original disease. According to Nencki and Sieber[1] hæmatoporphyrin and bilirubin are probably of synchronous production—their seat of formation being the liver cells especially. The readily convertible hæmatoporphyrin is utilized for the synthesis of the hæmoglobin molecule; the non-utilizable bilirubin is excreted with the intestinal contents. These deductions stamp the hæmatoporphyrin as a normal intermediary product of metabolism. Other investigators, however, have concluded that inasmuch as the normal bile does not exhibit hæmatoporphyrin, this does not seem to play an important role in the organism, and that it must not be considered an intermediary product of the anabolism or an essential catabolic product in the physiological disintegration of the coloring matter of the blood.

To determine the place of the abnormal production of hæmatoporphyrin, the individual organs of animals poisoned with sulphonal were examined for the presence of hæmatoporphyrin. This was never found in the spleen, blood, muscles, or marrow, but it could always be demonstrated in considerable amounts in the liver. However, as the liver is an important excretory organ of hæmatoporphyrin, its occurrence therein is by no means proof of its hepatogenous formation.

That hæmatoporphyrin was not the result of any of the remedies, there can be no doubt. Plumbism could also be positively excluded. We may assume, therefore, that if the hæmatoporphyrin was of toxic origin, the toxiferous substance was of intrabiontic origin. Whether the same toxic substance stands at the foundation of the accompanying or alternating symptoms, icterus and glycosuria, is a mooted question. I am inclined to accept the interrelation of the three symptoms in this instance. This is confirmed by the fact that while abnormal hæmatoporphyrinuria was present, the glycosuria, which had existed to a greater or lesser degree for some years previously, had ceased entirely, and that after disappearance

[1] Arch. f. experim. Path. u. Pharm., 1888, 24.

of the abnormal amounts of hæmatoporphyrin (how soon after could not be determined as no urinary examination was made between April 20th and May 14th), the glycosuria reappeared, occurring probably in greater intensity than ever before. It appears almost as if one and the same anomaly was the causative factor of the three manifestations, that while icterus set in when chronic glycosuria was present, this disappeared when hæmatoporphyrinuria supervened, and did not recur until the hæmatoporphyrinuria had again vanished. It seems that the disappearance of the glycosuria was dependent upon the presence of the hæmatoporphyrinuria; that is, that the anomalous condition underlying both symptoms could only bring about either of them at one time.

The case stands isolated, as I have not found in medical literature any allusion to the synchronous or respectively the intercurrent occurrence of these three phenomena. Operative interference may be required to relieve the tension of fluid in the gall-bladder. A more detailed study of the case will follow at a later day.

AN UNUSUAL OVARIAN CONDITION.

By Lewis Schooler, M.D.,
of Des Moines, Iowa.

The patient, whose case is here reported, was the wife of a miner and has been brought up amid the surroundings of the ordinary coal-miners' camp, with nothing of importance in either the family or personal history. She was the patient of Dr. Charles F. Smith, and I saw her in consultation with him about three weeks previous to time of the first operation. At that time she believed herself pregnant and sought an examination for the purpose of ascertaining whether she would be able to carry the child to term.

After a careful and painstaking examination I advised her to the effect that her pregnancy would not be interfered with by what I then believed to be a diseased Fallopian tube, but which I now know was an extensively drawn-out left uterine cornua. My opinion was most unsound, as she miscarried about ten days later and at a little more than the third month. This accident was not followed by any bad results, and she recovered very nicely after the miscarriage.

Urinary examination showed that fluid to be acid in reaction, specific gravity 1016, color light amber, cloudy, total solids 37.28 grams per 1000 c.c., albumin and sugar absent.

Mrs. W., aged twenty-four years, married, mother of two children, previous health good, entered the Methodist Hospital August 21, 1903. Condition at time of admission was as follows: Tem-

perature 98.4°, pulse 59, respiration 18; on the day following the temperature at 10 A.M. was 99.6°, pulse 80, respiration 24, and at 4 P.M. temperature 99.4°, pulse 66, respiration 19. Bowels moved freely after the administration of one ounce of castor oil.

From this date until August 27th there was not much change in the patient's condition except that pain, increased pulse rate with slight elevation of temperature, became gradually more marked, and the tumor in left side enlarged perceptibly; the bowels acted fairly well, but were assisted by castor oil every other day, and as there seemed to be no hope of improvement under medicinal treatment, operation was had on the 27th. The incision was begun in the median line a little higher than the point usually selected for an ordinary ovariotomy.

When the fingers were introduced it was discovered that the uterus was dragged upward and to the left, and the Fallopian tube felt like a firm round cord double its normal size, extending from the uterus to the enlarged and displaced spleen, which was firmly attached and admitted of no displacement. The incision was extended upward and the spleen brought into view. It was at least six times its normal size, black and glistening like an old blood clot, but firmer.

The hand was swept entirely around its base, which left no doubt as to the identity of the organ, but in order to further demonstrate the certainty of the diagnosis the capsule was opened and a small piece removed for microscopic examination, which resulted in confirmation of what has been stated above. At the lower pole there was complete and firm union of the spleen, ovary, and fimbriated extremity of the tube. So close was this union that it required close inspection to identify the different structures. The tube, ligament of the ovary, and the upper edge of the broad ligament, were hard and firm on account of the tension. It was then decided to divide them between two ligatures and close the abdomen, and while this was being done it was found that the spleen was bleeding rather freely from incised point and required packing with gauze. Healing by first intention occurred throughout, except where the gauze protruded.

The patient left the table in good condition at 3 P.M., the operation having lasted but thirty minutes, but at 5 P.M. the pulse was 112, and at 12.30 A.M. it was 140, and went up to 146 at 2 A.M., which was the extreme reached at any time. The temperature was 101°. Morphine, required on account of pain, and normal saline solution in large quantities were given at this hour. The pulse improved, and at 8 A.M. was 120; temperature 100°.

From this time there was nothing of interest in the case and she left the hospital September 11th.

Four weeks later she was seen at her home and was suffering from obstruction of the bowels, which disappeared on the following

day. At this time the spleen was apparently reduced in size at least one-half. She was admitted to the Mercy Hospital November 17th with complete obstruction of the large intestine, and was operated on at once, the incision being in the left semilunaris.

The obstruction was due to extensive adhesions almost the entire length of the descending colon. They were ligated at several points and the bowel freed and filled with normal saline solution through the rectum. The uterus was normal in size and position. The spleen was in like condition and, instead of the intensely black color present at the time of the first operation, was normal in appearance. The patient made a good recovery and left the hospital on November 30th in apparently good condition, with the bowels acting normally and free from pain. To me this experience is unique.

How two organs normally so far apart and with a limited amount of mobility got together and stayed together, I cannot explain. If it was a wandering spleen, what caused it to return to its normal site, and up to the present time to remain there? The patient had never suffered from malaria and the blood count showed no anomaly in that direction.

Previous to the second operation, I was perfectly contented with the explanation of a floating spleen, but the revelation of the last operation has caused me to give up that theory.

STUDIES UPON THE CAPSULE OF THE KIDNEY.

By Haven Emerson, A.M., M.D.,
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From the physiological standpoint, the fibrous envelopes or capsules of organs have received but scant attention, and it was a desire to make some addition to the facts known about such capsules that led me to make the following studies.

Among the organs studied the results obtainable have been most definite in the case of the kidney, partly because of the distinct existence of the kidney capsule, and partly because of the greater convenience of manipulation, due to the size and location of the organ, than is the case with other organs, such, for instance, as the pancreas or the submaxillary gland.

Observations upon the capsule of the kidney have become especially interesting, in view of the present discussion of surgical procedures which depend for their effect upon an alteration of the normal relations of the capsule and its blood supply to the functions

and structure of the kidney parenchyma. The following studies were made upon dogs, rabbits, and a pig:

The capsule of the kidney is made of firm connective tissue with a moderate amount of yellow elastic fibres. It is arranged in two layers, the outer thick and dense, the inner represented often by only a single layer of cells. The inner layer is always adherent, even when the capsule is roughly removed, and is continuous with the intertubular connective tissue. Vascular connection with the peritoneum covering the capsule is slight, the main blood supply to the capsule being from the kidney parenchyma by abundant bloodvessels of considerable size, distributed irregularly over the surface of the kidney. The capsule seems to serve as a support, and as a protection against injury and pressure from without.

My first experiments were devised to ascertain whether the capsule would allow or prevent the absorption into the blood of salts in solution. My second series aimed at determining the result of decapsulation of the kidney, upon the animal and the organ.

Part I.

Medium and small dogs were used, 5 to 9 kilos in weight. Males were preferred because the internal generative organs of the female make the catheterizing of the ureters difficult. The animals were kept on a fluid diet of soups and milk for forty-eight hours before the operation.

Various containers for the kidney were tried, in which the kidney might rest immersed in a liquid and yet suffer no constriction of its vessels and ureter at the hilus, while at the same time allowing no escape of liquid into the peritoneal cavity at large. The only satisfactory object was found to be an oblong bag of rubber tissue.

Ether narcosis was used, often preceded by a small subcutaneous dose of morphine sulphate (0.4 to 1.0 dg.). Tracheotomy was performed in all cases for convenient anæsthetization. With the animal in the dorsal position a median abdominal incision was made from the ensiform cartilage to the penis, with a lateral incision at right angles to the former cut, just below the free border of the ribs on the left side, the left kidney being more conveniently located for experiment than the right. The kidney was then exposed. Its peritoneal coat and fat were stripped off to the hilus, and then, with or without decapsulation, the organ was enclosed in the rubber bag. The removal of the capsule was done by elevating a portion with a sharp hook, cutting under the hook and separating the capsule from the parenchyma with a blunt, flat, smooth seeker. The open end of the rubber bag was passed over the kidney and clamped about the hilus, leaving vessels and ureter ample room. The bag was then drawn back until it fitted the kidney snugly, leaving the hilus free, about three-fifths of the sur-

face and bulk of the kidney remaining within the bag. The blind end of the bag was fitted with a glass tube, over which a short piece of rubber tubing provided with a clamp was slipped. The bag was then filled with 50 c.c. of warm normal saline solution, and the kidney was allowed to assume its normal position. One or both ureters were catheterized by glass tubes, bent so as to empty into test-tubes near the dog's side.

If it was found, then, that all bleeding from the surface of the kidney had ceased, that there had been no leaking from the bag, and that the kidney was secreting, the saline solution was drawn off, the bag was filled with the test solution, and the urine was collected at short intervals and tested. The phenomena observed on stripping the capsule from the kidney are described in Part II.

Of the twenty-four animals used for these experiments the results had to be thrown out in two cases because of leaking of the test solution from the bag into the peritoneal cavity. Control tests were always made of the peritoneal fluid to prevent error from possibility of absorption through the peritoneum instead of the kidney. In four cases I failed because the bag was too tightly applied, and constriction of the parenchyma caused compression of urine; in two cases because the intestines were too much distended to allow of delicate manipulation; in one case because of uncontrollable bleeding from an abnormally located renal vein. The remaining fifteen gave the following results:

Potassium iodide was used with three animals upon kidneys possessing normal intact capsules, in solutions of 1 per cent. and 10 per cent. for one-half to two hours, and in no instance was iodine found in the urine (the test for iodine being made with fuming nitric acid and chloroform). In two animals the same strength of solutions were used upon kidneys possessing newly formed capsules thirty-nine and forty-four days after decapsulation, with the same negative results.

For the sake of brevity the term normal kidney will be used to signify a kidney possessing an intact capsule as distinct from a decapsulated kidney. No diseased kidneys were found.

Similar solutions were used upon the freshly decapsulated kidneys of two animals, and iodine was found in the urine in twenty minutes. In two animals potassium iodide in 10 per cent. solution to the amount of 100 c.c. was injected into the femoral veins, while the bag enclosing the freshly decapsulated kidney contained normal saline solution. The saline solution was tested at intervals for one and one-quarter hours, and, although there was an abundance of iodine in the urine, none appeared in the solution in the bag.

Sodium salicylate in 10 per cent. solution was applied by means of the bag to the normal kidney for one and one-half hours with negative results. A similar solution applied to the freshly decapsulated kidney resulted in the appearance of the salt in abundance

in the urine in twenty-five minutes. In a 1 per cent. solution, applied for one and three-quarter hours, to the decapsulated kidney, the sodium salicylate did not appear in the urine. In the last two cases the secretion of urine became distinctly diminished on application of the solution of sodium salicylate, and this diminution reached such a degree in the last case that not enough urine was secreted to afford a test after the first half-hour, there being a cessation of secretion without any congestion to account for it.

Potassium ferrocyanide in 10 per cent. solution was applied to the normal kidney with negative results. Applied to the freshly decapsulated kidney, its presence was detected in the urine in forty-five minutes.

Potassium cyanide in 0.6 per cent. solution was applied to the normal kidney with no effect upon the general condition of the animal. When a 3 per cent. solution was applied to the normal kidney, irregular and frequent heart beat and shallow, feeble respiration were noted in a half-hour. The 0.6 per cent. solution was used upon a freshly decapsulated kidney, and in ten minutes there was a marked irregularity of the heart action and respiration. The solution was then removed and the animal recovered.

Methylene blue in saturated solution and in solution of 1 per cent. and $\frac{1}{60}$ per cent., when applied to the normal kidney, gave no evidence of its absorption during two hours. When tried upon the freshly decapsulated kidney for the same length of time the same solutions also gave negative results. When 60 c.c. of a $\frac{1}{60}$ per cent. solution were injected into the femoral veins no blue color appeared in the clear saline solution in the bag surrounding the decapsulated kidney, although the urine secreted during the time of observation was deeply stained. Immediately after the exposure of a freshly decapsulated kidney to a saturated solution of methylene blue for two hours the kidney was removed and frozen sections were cut and examined at once. A thick, superficial lymph clot, which forms on the surface of the kidney after decapsulation, was found to be stained blue, and there was a delicate staining of the connective tissue of the parenchyma as far as the more superficial glomeruli.

SUMMARY OF PART I.

It is apparent that when the kidney capsule is intact absorption does not take place in sufficient amount to be appreciated by chemical tests in the urine, and that only when a strong solution of a powerful systemic poison was used was there any indication of the test substance in the blood stream, as shown by constitutional symptoms.

It is also evident that, when the capsule was stripped, of the five substances tested three appeared promptly in the urine; one, potassium cyanide, showed a marked constitutional effect, and one, methylene blue, failed to be appreciated in any way. It seems

likely that if the circulatory disturbance had not caused a marked cessation of urinary flow potassium cyanide would also have been absorbed into the renal tubules. With methylene blue the lymph clot formed upon the denuded kidney surface appeared much more quickly than with the other solutions employed. The surface through which absorption might occur was thus rendered much less accessible to the solution, and to this condition we must ascribe the negative result. The fact that there was a discoloration of the parenchyma as far as the glomeruli gives warrant for believing that absorption was under way, though in a slight degree. From the appearance of the surface of the kidney two to three hours after decapsulation, it would be hard to believe that more absorption would occur after that time than would take place with the capsule intact. It may be worth noting here that the results of my experiments suggest that the use of strong antiseptic solutions in the vicinity of a decapsulated kidney may do harm by direct absorption into the kidney parenchyma. They thus furnish a reason in addition to those accepted for surgical technique for limiting the fluids, allowed to come in contact with such an organ, to sterile water or physiological salt solution.

Part II.

While watching the experiments, already described, it was apparent that an attempt at repair of the injury inflicted by decapsulation was already begun in the half-hour to three hours while the dogs were under observation. The fifteen dogs which suffered decapsulation for the sake of immediate observation of absorption showed the various stages, from multiple hemorrhages, due to the rupture of the capsular bloodvessels, to the formation of a firm, smooth, elastic lymph clot, destined to assist in the formation of a new fibrous envelope. Except in rare instances, where there is unusual vascular distribution, the hemorrhage resulting from removal of the healthy capsule in the dog ceases in about five minutes. Exudation of lymph from countless points over the whole surface of the kidney follows decapsulation, and in a half-hour there is formed a smooth, clear, jelly-like coat. This film at first thickens unevenly, and then gradually becomes cloudy as the fibrin network is established, until at the end of two hours there is a firm, tenacious, slightly adherent lymph clot protecting the denuded surface. For the later effect of decapsulation we may turn to the following operations and autopsies:

Eight dogs, six rabbits, and one sow were used. Of the dogs I failed in one because of asymmetry of one of the renal veins, which entered high upon the side of the kidney instead of at the hilus; and in one from an error in following the muscular guide in my incision, and resulting hemorrhage. The remaining six showed no sepsis,

the wounds healing cleanly and promptly. There was at no time any abnormal condition of urine of any of the animals. They were autopsied at various intervals from thirty-nine to three hundred and thirty-nine days after operation, and without exception were in perfect condition when killed. (For the number of days after decapsulation in each case, see report of autopsy.) In the cases of the dogs the operation was by the lumbar incision. The kidney was drawn into the wound by its perirenal fat, and held there by pressure from below until the capsule was stripped, in the manner already described. It is a matter of some difficulty to decapsulate the kidney of a dog without entering the peritoneum, but in Cases IV. and V. especial care was taken, and in Case V. the whole operation was done extraperitoneally. This difficulty is due to the almost complete investment of the kidney with peritoneum, the perirenal fat being usually very scant.

Of the six rabbits, one died in four days from occlusion of the ureter, which resulted from an attempt to bind the decapsulated kidney to a lobe of the liver by silk sutures. Three of the remaining five were operated upon by the lumbar method, and the capsule stripped without entering the peritoneal cavity—a procedure not at all difficult in the rabbit. In the other two I opened the abdomen in the midventral line and decapsulated the kidney without precautions except as to injury of other viscera. Each of these rabbits developed a ventral hernia, due to the use of plain catgut in sewing the muscular layer of the abdominal wall. None of them suffered any sepsis or appeared otherwise than healthy, except for the presence of what appeared to be an eczema of the nose and skin of the face during the month before autopsy.

The operation upon the sow was done by a lateral abdominal incision, and the capsule was stripped intraperitoneally. The animal increased from one hundred and fifty to three hundred and fifty pounds between the time of operation and the date of autopsy.

At the time of autopsy several of the kidneys were injected with blue gelatin mass in the following manner: The kidney, with whatever structures or organs were adherent, was placed in a bath of 0.85 per cent. salt solution at a temperature of 99°. Cannulas were inserted into the artery and one vein at the hilus, the other vein or veins being then clamped. The kidney was then washed free from blood by forcing saline solution through first the artery and then the vein at a pressure of 180 mm. to 200 mm. of mercury and at the temperature of 99° to 100°. Then a thin gelatin mass stained deeply with Berlin blue was forced through under the same conditions of pressure and temperature for an hour or more by the artery and then for an equal time by the vein. The artery and vein were tied and the kidney was packed in ice until the gelatin had hardened.

All specimens were hardened in equal parts of Müller's solution

and 5 per cent. formalin, and the stains used were either hæmatoxylin and eosin or the carbol fuchsin.

The gross and microscopic findings upon the six dogs, five rabbits, and the sow follow:

CASE I.—Mongrel, adult male, 10.5 kilos, thirty-nine days after decapsulation of the right kidney intraperitoneally by the lumbar method. The left kidney presented nothing abnormal. Adhesions were found on the right side between the right kidney and the left lobe of the liver about one-half inch long, also to the omentum, the latter not only over the decapsulated area, but at the hilus as well, where only the peritoneum had been stripped. Slight bleeding occurred on separating the adhesions, and this, apparently, wholly from the liver and none from the kidney. The animal was kept under ether an hour to study the circulation. The newly formed covering of the kidney was found more adherent than normal, though quite soft and tearing the parenchyma slightly when stripped.

Microscopic. The normal kidney shows an even capsule, an inner thin cellular layer, and an outer thicker fibrous connective-tissue layer. The decapsulated kidney shows a newly formed connective-tissue envelope, in some places thinner, elsewhere from three to five times thicker than normal. The outer layer has abundant round cells loosely embedded in young connective tissue. The inner layer still marked, evidently not stripped off at the operation, but its character much less distinct at the site of the adhesions, where it appears to have been absorbed, and where occasional wedges of round cells are seen crowding among the urinary tubules. The whole newly formed coat appears but slightly vascular. No changes appear in the renal parenchyma.

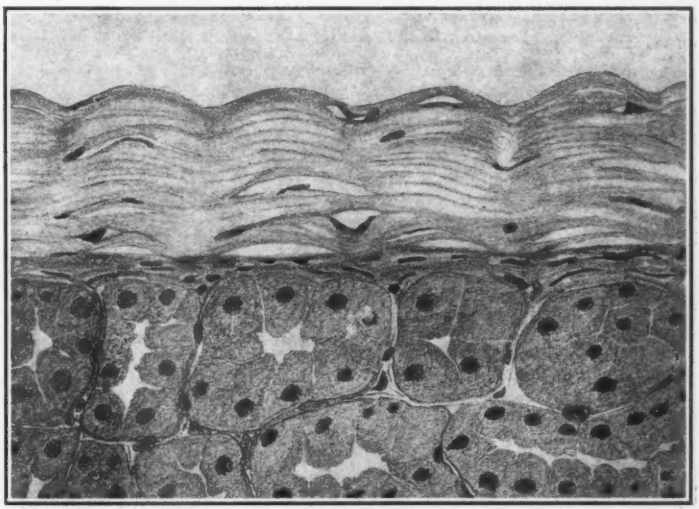
CASE II.—Adult male fox-terrier, 8 kilos, autopsied one hundred and forty-four days after decapsulation of the right kidney intraperitoneally. Left kidney showed nothing abnormal. (See Fig. 1.) Firm adhesions were found between the right kidney and the left lobe of the liver, the pancreas, the mesentery, and the large intestine. Marked absence of bleeding was noticed on tearing the attachments except where the pancreas is adherent. This attachment is so close that it cannot be separated without tearing off the newly formed capsule. The surface of the kidney is irregular, appearing like the granular kidney seen in chronic interstitial nephritis in man. The capsule cannot be removed without tearing the parenchyma.

Microscopic examination shows essentially the same variation from normal as in Case I., with the following differences: The inner capsular layer is strikingly absent where adhesions are formed and especially at the site of the pancreatic attachment. Elsewhere the inner layer is thicker than normal. The outer layer and capsule as a whole are everywhere much thicker. (See Fig. 2.) Small, newly formed vessels, such as are found in granulation tissue, are

seen in loosely arranged connective-tissue bundles between the pancreas and the kidney. Tubules which reach the surface of the kidney are in places distorted and crowded by the encroachment of connective-tissue cells, this invasion of the parenchyma in some places taking form of distinct wedges. In some places are found cup-shaped depressions, with destruction of considerable areas of tubules and glomeruli, the whole degenerated tract appearing strangled by the network of contracting connective tissue.

CASE III.—Small male, mongrel puppy, 5 kilos. Examined two hundred days after decapsulation of the right kidney intraperitoneally. The left kidney appears normal. Adhesions to the pan-

FIG. 1.



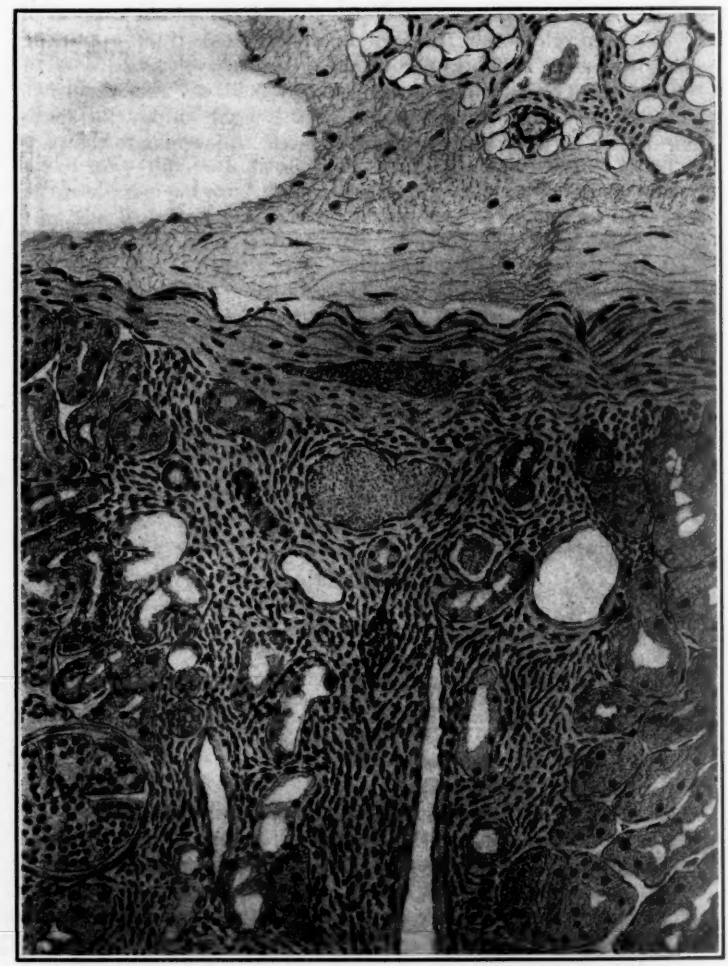
Normal (left) kidney of Case II.

creas, the liver, and the posterior abdominal wall almost completely cover the kidney surface. The viscera are connected not by bands, but directly surface to surface. The muscular attachment is by a dense, non-vascular band impossible of separation without tearing off the newly made capsule and some of the renal parenchyma. This kidney was injected with gelatin mass, as described above. From the cut surfaces of the pancreas and liver the blue mass flowed freely during the whole period of injection.

Microscopic examination shows the following: A section of the kidney at a point where no adhesions were formed shows a much thickened capsule of new dense connective tissue, with small blood-

vessels injected with the blue gelatin mass directly connecting with the capillaries of the renal parenchyma. Deep wedges of round

FIG. 2.

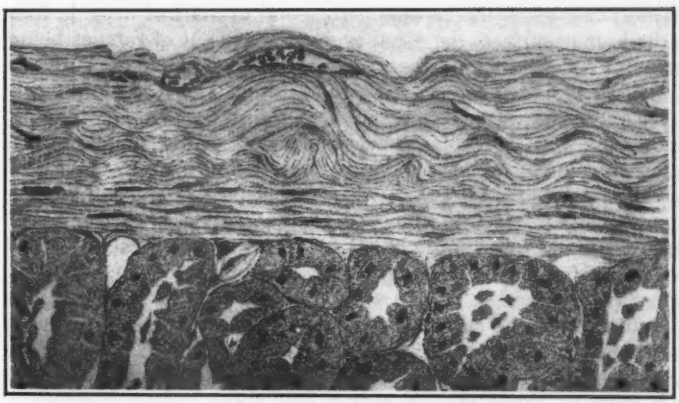


Decapsulated (right) kidney of Case II., showing thickened capsule.

connective-tissue cells enter from the capsule as far as the nearer glomeruli.

A section at a point where the liver is in intimate contact with the kidney shows in some places a thin layer of dense connective tissue of the thickness of the inner layer of the normal capsule, and no vessels communicating between the two viscera. In other places is seen a marked injection of liver capillaries and also injected vessels in the connective tissue between the two viscera. At some points there are but two extremely thin layers of flat connective-tissue cells separating the viscera from each other. At frequent points along the renal cortex are seen deep connective-tissue wedges distorting, destroying, and occluding the tubules, and in some instances even completely surrounding the glomeruli. Degeneration of the tubular epithelium is present in all such areas. (See Fig. 3.)

FIG. 3.



Decapsulated (right) kidney of Case III., showing cup-shaped depression with tubular and glomerular degeneration and replacement fibrosis.

Where the pancreas is adherent to the kidney the connective tissue separating them is thicker than where the liver is adherent; otherwise the conditions are the same. Blue injection mass is seen in the smaller vessels and capillaries at various points in the pancreas.

CASE IV.—Brown and black mongrel, 7.5 kilos. Autopsied two hundred and forty-five days after extraperitoneal decapsulation of the right kidney. To ensure the kidney remaining in position three plain catgut sutures were used at the time of operation to bind it to the muscular wall at the site of the wound.

Through the courtesy of Dr. Isaac Levene I had an opportunity to observe oncometric records of this kidney with and without the use of adrenalin intravenously. The character of the tracings was

identical with that of the tracings from a normal kidney under the same conditions.

The only attachments were to the perirenal fat and the muscular wall of the abdomen.

The left kidney showed no alterations of the capsule or of the parenchyma, the inner layer of the capsule being about one-half to two-thirds the diameter of a convoluted tubule in thickness, and the whole capsule two and a half to three and a half the same diameter. No interstitial infiltration or epithelial degeneration.

The right kidney has a capsule freely supplied with large and small vessels, some with well-defined walls. The blue gelatin mass shows free connection between the intertubular capillaries and the blood spaces and vessels in the loose reticulum of the new capsule. The new capsule varies from normal thickness with a very dense structure to a loose network as much as fifteen times as thick.

Unevennesses of the capsule correspond to marked irregularities in the kidney surface, the usual even arrangement of tubules being broken by depressions, where connective-tissue processes invade the parenchyma.

There is a uniform degeneration of the outer layer of tubules, accompanied in some places by absorption. A few glomeruli are found surrounded by new connective tissue. The deeper layers of the kidney appear natural. Upon the surface of the kidney are found abundant tufts of young connective tissue with a free blood supply running into the perirenal fat. Where the capsule is relatively thin and dense the blood supply is scanty, quite as few blood spaces being found as in a normal capsule.

At the site of the adhesion to muscle there is a mass of connective tissue of a firm type with a free vascular supply. In this area, 5 x 7 mm., the tubules are distorted, compressed, and drawn up, as it appears, out of the adjacent kidney tissue by the contracting connective tissue. Compression, flattening, and degeneration of tubules and glomeruli are seen in bulk. This is probably the location of one or more of the retention sutures. Adjacent to this area is a part of the capsule which shows no variation from normal in thickness or vascular supply and could not be distinguished from normal except by a lack of definiteness between the inner and outer layers.

Case V.—Black mongrel, 7 kilos. Autopsied two hundred and fifty-one days after decapsulation of the left kidney. Care was taken to do this decapsulation extraperitoneally, but without success. The dog was pregnant at the time of the autopsy.

The left kidney was adherent to the muscle of the wound and to the mesentery.

The right kidney appeared normal, and on section showed no variations from normal in capsule or parenchyma.

The left kidney shows an uneven capsule varying from one-half

to four times normal thickness, except at the site of the attachment to the muscle of the lumbar wound. Vascularization of the capsule generally is slight, the tissue being dense and with but few round cells. The adhesion between the kidney and the muscle is 2 mm. long, highly vascular, with a few masses of dense connective tissue. At this point connective-tissue invasion of the parenchyma is noticeably greater than elsewhere in this kidney.

CASE VI.—Small brown terrier, 6.5 kilos. Autopsied three hundred and thirty-nine days after decapsulation of the left kidney intraperitoneally. This dog had had a litter of pups, and was again pregnant at the time of autopsy.

The right kidney shows no variations from normal in the capsule or the parenchyma.

A few adhesions to adjacent fatty tissue were found, but none to any viscera from the left kidney.

The left kidney shows a firm, fairly even capsule for the most part, but slightly thicker than normal. At places, however, the capsule is as much as five times the normal thickness. Blood-vessels are very rare in the firm, thin parts of the capsule, and are present in fair size and number only where the capsule is thick and loosely constructed. Young round cells are present only in the thicker parts. In other words, over the greater part of the kidney we find a capsule resembling the normal intact capsule in every respect, except in the definiteness of the layering of its tissue. It is, however, to be noted particularly that exactly where the abnormal thickness and vascularization of the capsule persist we find the invasion of the parenchyma by connective tissue with resultant degeneration and atrophy of the tubules.

Everywhere, even under the more normal-appearing capsule, are evidences of pressure and contraction, causing an unevenness of the cortical layer of tubules.

CASE VII.—Brown and white buck rabbit, autopsied fifty-nine days after decapsulation of the right kidney.

CASE VIII.—Slightly larger brown and white buck rabbit, autopsied eighty-four days after decapsulation of the right kidney. The gross appearances are identical in both, there being no adhesions to other viscera, as the operations were wholly extraperitoneal. The perirenal fat is more firmly bound to the operated than to the normal kidney. A slight milkiness and a perceptible difficulty in stripping the newly formed capsule were all that distinguished the operated from the normal kidneys.

Microscopic examination of Case VII. shows the layers of the normal capsule less marked than in the dog. The newly formed capsule presents the characteristics of young connective tissue. It is thicker than normal by four or five diameters. Round cells are abundant throughout. No vascular connections with the parenchyma are found, and there is no infiltration of the parenchyma with

connective-tissue cells. The new capsule has formed under the intimately attached perirenal fat. Microscopic examination in Case VIII. shows exactly the same state of things, except that the outer layer of the new capsule is denser and the cellular elements are less marked.

Case IX.—Adult brown buck rabbit, autopsied one hundred and forty-eight days after decapsulation of right kidney by the abdominal intraperitoneal method.

The left kidney was normal in its relations, and on microscopic examination showed normal capsule and parenchyma.

The right kidney was adherent to the intestines by loose bands of connective tissue and to the liver, intimately, surface to surface. The newly formed capsule is made of loose, young connective tissue with a few areas of much thinner, denser tissue, especially at the site of the adhesions to the liver. Where the capsule is of loose structure there are a few small capillaries, but elsewhere the capsule appears about as little vascular as in a normal capsule. There are few regions of penetrating connective-tissue wedges, but these are characterized by all the usual appearances, and the tubules at the cortex are very generally the seat of cell degeneration. At a few points over the surface of the liver attachment there is an invasion of connective tissue among the liver cells, with resultant cell degeneration. There was no evidence of vascular connection with the liver, although the capsule at several points, where it is loose and thick, shows frequent injected vessels.

Case X.—Adult brown buck rabbit, autopsied two hundred and forty-one days after decapsulation of the right kidney by the abdominal intraperitoneal method.

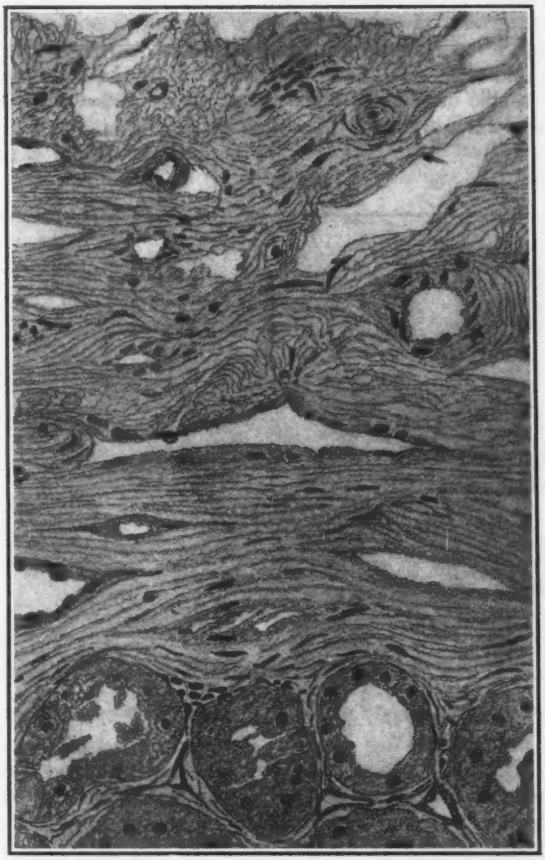
The left kidney is normal in every respect—macroscopically and microscopically.

The right kidney is adherent to the under surface of the liver and very firmly to the fatty capsule. No marked vascular supply. Section through liver adhesion shows slight injection of liver capillaries at several places, with occasional small vessels in the thick capsule. The capsule varies from one-third to six times normal in thickness, and is characterized by dense and non-cellular structure. There is no intertubular interstitial increase, but the tubules are dilated and filled with cell detritus; the epithelium is flattened, and the nuclei stain poorly and lack definiteness. These changes are less marked the farther we go from the cortex. The glomeruli are not affected. Where the absorption of the new capsule between the liver and the kidney had gone so far as to leave but a single layer of spindle-shaped cells, there were several small masses of round cells invading the liver substance.

Case XI.—Gray female rabbit, autopsied two hundred and seventy-five days after decapsulation of the right kidney by abdominal intraperitoneal operation.

The left kidney presents no variations from normal. (See Fig. 4.) The right kidney shows a few light adhesions to the fatty capsule and the mesentery.

FIG. 4.

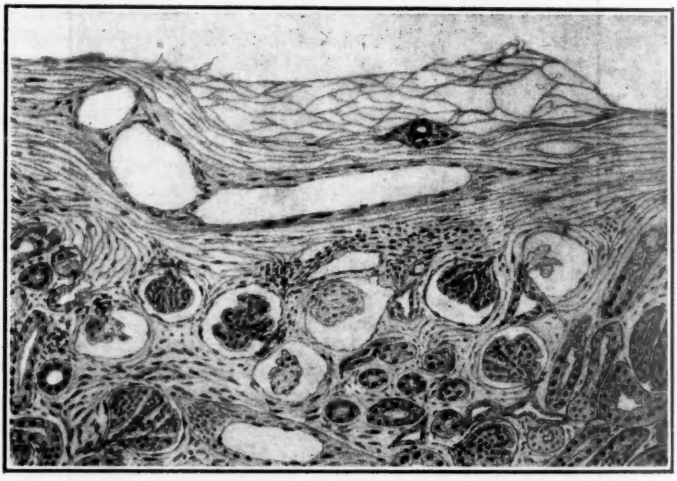


Normal (left) kidney of Case XI.

Everywhere over the surface of the kidney, except at the site of the few adhesions, the capsule varies but slightly from the normal in thickness. Where the capsule is of normal thickness the structure is denser and slightly more cellular, but no more vascular than normal. The adhesions are well supplied with organized blood-

vessels. The parenchyma has suffered severely. In a section exposing one-third of the transverse circumference of the kidney are found seven distinct wedges of new, round-cell connective tissue invading the cortical tubules from the capsule. Three of these wedges extend half-way to the hilus, and are lost in the intertubular tissue among the straight tubules. In the path of these tracts are found all grades of compression and degeneration of tubules and glomeruli, from a cloudiness and constriction of the deeper tubules to a complete replacement fibrosis just beneath the capsule. There is a noticeable increase of bloodvessels in size and number in these connective-tissue wedges. (See Fig. 5.)

FIG. 5.



Decapsulated (right) kidney of Case XI., showing a typical connective-tissue wedge.

CASE XII.—White sow, autopsied two hundred and forty days after decapsulation of the left kidney by the abdominal intraperitoneal method.

The right kidney is normal in every respect. The capsule resembles the rabbit kidney in being loosely attached and thin. Evenness of arrangement of the tubules and a full regular and sharply defined appearance of the tubular epithelium characterizes the parenchyma.

The left kidney has light adhesions to the perirenal fat, to the mesentery, and to the omentum. These are tough and do not bleed when torn. Changes are seen in the capsule similar to those noted in the decapsulated kidneys of other animals. Uneven thickening

varying from two to ten times the normal thickness, and an irregular and occasionally free vascular supply, less where the capsule is densest and where there are no adhesions. Vessels can be made out communicating between the capsule and the adhesions. In the parenchyma there is a widely distributed round-cell infiltration from the capsule, deep among the tubules, with occasional wedges penetrating farther among the glomeruli. Cellular degeneration is not found to a great degree among the tubular epithelium, but there are regions, chiefly at the surface of the kidney, where the effect of pressure is shown by disintegration of cell bodies. Where the interstitial increase is greatest are found more abundant intertubular vessels, but it is with difficulty that even small vessels are to be found penetrating the capsule from the parenchyma of the kidney.

Reports of Previous Experimental Studies.

Without entering the tempting field of medical speculation as to whether decapsulation does or does not benefit the kidney, already the seat of a chronic inflammatory condition, I shall confine my report to the results of experimental investigations undertaken to assist the clinician and the surgeon.

Albarran and Bernard[1] studied the kidneys of rabbits from fifteen to sixty days after decapsulation by the lumbar method. They found a few minor changes of degeneration in the tubules near the surface and the prompt formation of a new capsule denser than the original. They conclude that the effects of relieving congestion by decapsulation of the kidney, claimed by some operators, must be transient when the rapid re-formation of a denser capsule so soon follows the removal of the original one.

Boutch-Osmoloffski[4] also studied rabbits after decapsulation by both the lumbar and abdominal method. He found marked proliferation of new connective tissue into the parenchyma within six days after decapsulation of the kidney. Twelve days after decapsulation he found marked connective-tissue growth, but not deeply into parenchyma. He found that the kidney tissue at the surface undergoes marked atrophy and replacement fibrosis, but found no newly formed vessels.

Johnson[9] found in dogs that decapsulation of the kidney results in the formation of a new fibrous capsule usually thicker than normal, but varying greatly in thickness. He found occasional infiltration of round cells into the renal cortex, but no effect upon the glomeruli. He found no anastomoses between the renal and the perirenal bloodvessels. He concludes that there is no experimental evidence to support the vascular hypothesis for the cures claimed in cases of chronic Bright's disease, treated by decapsulation of the kidney.

On the other hand, Bassan,[3] in his very complete monograph on surgical intervention in medical nephritis, says that decapsulation

appears well adapted as a surgical treatment of Bright's disease, because of the probable creation of new paths of blood supply to the diseased organ. Without giving any facts to support this statement he says that his own, as well as the experiments of Claude and Balthazard,[5] favor this view.

Claude and Balthazard[5] do claim to have found important venous and lymph channels in the organized perirenal adhesions, but they give no definite proof that these vessels actually communicated with the renal parenchyma. They state explicitly, however, that although urinary secretion is maintained well and with less cardiac exertion after decapsulation than before, if improvement is to follow, we must have normal epithelium, or else the relief from circulatory pressure will be of no avail. The cases of Claude and Balthazard were studied twenty-five to thirty days after decapsulation.

Fabris[7] concludes from experimental decapsulation in animals that a new capsule is formed in thirty days. This capsule is firm and tough, and has but a slight additional supply of new blood-vessels. He adds that decapsulation may help a unilateral acute nephritis, but that in bilateral and chronic disease it can but be of little or no value.

Ferrarini[8] concludes from numerous experiments upon healthy animals that decapsulation of the kidney causes no functional disturbance or anatomical lesion. The newly formed capsule results from perirenal inflammation accompanied by vascular connection from the capsule to the stellate and medullary veins of the kidney.

In a series of decapsulations of rabbits' kidneys, after acute degenerative processes had been established by the use of irritant drugs, he concludes that there are no essential differences between the normal and the operated kidneys. The observations were made from six to sixteen days after decapsulation.

Anzilotti[2] observes in dogs and rabbits that a new capsule is formed in fifteen to twenty days after decapsulation. In various cases from twenty-four to one hundred and fifty-eight days after decapsulation he finds the new capsule thickened, the tubules distorted, and their epithelium degenerated, the glomeruli undergoing necrosis, and new vessels in the kidney tissue and the capsule.

In a second series he caused a degree of replacement fibrosis in the kidneys by temporary interference with the renal blood supply, and subsequently decapsulated one kidney. He concludes that decapsulation may cause a notable improvement in such a kidney by improving the circulation and causing a regeneration of kidney tissue.

The observations were none of them over a longer period than the cases noted by him in normal kidneys.

Anzilotti's report of observation of regenerated epithelium seems a little fanciful and is not supported by any illustrations of the

tissues so affected. If this degeneration takes place as Thorel[11] also thinks, even in two to eight days after the use of chromic acid or bichromate of potassium as an acute poison, he sees it occur without decapsulation—a fact which, if correctly observed, would scarcely argue for decapsulation.

In regard to the freedom of circulation through the kidney immediately after decapsulation, reference to the oncometric results reported by Dr. Levene[10] show that this is very marked for one or two days after decapsulation, but a similar test made on Case IV., reported above, showed that at any rate in two hundred and forty-five days such increased freedom has again been contracted to normal limits.

Summary of Results.

Evidence from various sources based on observations of kidneys in various animals from five to three hundred and thirty-nine days after decapsulation conclusively proves that decapsulation of a normal kidney may cause an interstitial nephritis of greater or less extent, varying from a simple invasion of parenchyma with connective-tissue processes in the early cases, to marked and advanced replacement fibrosis, and accompanying degeneration of renal epithelium in the tubules, and, occasionally, even atrophy and destruction of the glomeruli.

There are usually found, sooner or later, after decapsulation, some new blood channels between the kidney and the new capsule, and between the capsule and tissues or organs which may have become adherent. The conditions favorable to this production of new bloodvessels are: an intraperitoneal operation, the injury of adjacent tissues, the formation of natural or induced cicatrices, and a certain length of time after operation. These vessels when formed apparently increase in size and number according to the amount of connective tissue in the adhesions or the capsule to be nourished; they then appear to be gradually compressed with the contraction of the connective tissue, and the greater firmness and denseness of the newly formed capsule, until their number is inconsiderable and their size greatly reduced, so much so as to show no striking differences from the vascular supply found in a normal intact capsule.

The thickness of the new capsule and the abundance of bloodvessels seem to be accompanied in proportion by an increase of the connective-tissue infiltration and by a parenchymatous degeneration of epithelium. When the decapsulation is performed extraperitoneally the vascular new-growth is at its minimum, the interstitial increase in the parenchyma is not noteworthy, and the only evidence of change in the kidney is the contraction of the new fibrous envelope upon the kidney, causing an unevenness of its surface.

The preliminary report of this work made a year ago[6] indicated the results above stated, and I feel now that it is right to say that after decapsulation of a kidney we may hope for a temporary relief from pressure; and if under the proper conditions we may expect an increased vascular supply for a limited period. But we must face the certainty of the formation of a quickly forming, dense, and contracting capsule; the probability of the establishment of a chronic interstitial nephritis in the majority of the cases, and only a possibility of any permanent increase of the renal blood supply.

As a tribute to the successful healing of a severe lesion, such as decapsulation causes, it is fair to state that the newly formed capsule is efficient to protect the kidney from absorption from without, and from extremes of vascular pressure from within. Certainly the possibility of attaining more than a temporary improvement of a diseased condition of a kidney by decapsulation would appear slight.

The theory that an increased vascularization of the kidney formed by the development of contracting scar tissue is able to accomplish a gradual absorption of the interstitial connective tissue among the tubules and glomeruli, thus freeing them from pressure, may be justifiable from the clinician's standpoint, but it has scanty encouragement from experimental research.

CONCLUSIONS.—Decapsulation of the kidney in healthy animals may and usually does cause an interstitial nephritis.

New bloodvessels are formed in such adhesions as occur, these vessels being of but temporary character, as they are later occluded by the contraction of the cicatricial tissue surrounding them.

The ultimate result is a newly formed capsule not differing essentially from the original one, except in its tendency to persistent and uneven contraction.

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ON THE EARLY HISTORY OF CEREBRAL LOCALIZATION.

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If we read even superficially the writings of the ancient, mediæval, and early modern physicians I think we will find ourselves asking the question, Why is it that information concerning the nervous system, its anatomy, physiology, and pathology, remained so meagre in comparison with knowledge upon other subjects? Surely there were many instances of nervous disease, and competent observers were not wanting. Sydenham, Harvey, Cullen, the Hunters and Graves, not to mention others, would assuredly have contributed more to our knowledge than they have, were it possible in their age to do so. The explanation of this as of every other phenomenon in the course of thought is to be looked for, I believe, in the intellectual history of the times. Men, for various reasons, were not prepared to understand the nervous system, and among several it would seem that four causes have a special significance: first, an erroneous physiology of the brain; second, the absence of anything approaching to a comprehensive anatomy of the brain, and in particular of its convolutions; third, a speculative philosophy that was content with purely *a priori* explanations of nervous activity; fourth, the lack of an adequate scientific method. To these causes we may, perhaps, add the more general one referred to by Sir William Hamilton, who says: "Of all subjects of scientific interest men in general seem to have weakest curiosity in regard to the functions of their own minds and even bodies. So it is now, and, however marvellous, so it has always been." The influence of each of these factors will appear more plainly as we proceed.

When men began to reflect about themselves and to analyze the content of their consciousness, one of the first results must have been a localization of activity in the various organs of the body; and this is, in fact, what we find. The ancients localized digestion in the alimentary tract, respiration in the lungs, and in a vague general way the intellectual faculties in the brain, although the intimate relation of the thoracic and abdominal organs with the emotional tone of activity often resulted in the reference of mental acts or moral feeling to the heart, the liver, the spleen, or the bowels. Such a tendency may be observed among savage tribes as well as among the more cultured Egyptians and Hebrews, Persians and Arabians, Greeks and Romans. It has been crystallized in language and survives to our own day. We speak of training the heart as well as the mind, and the vagaries of our dyspeptic friend whom we have always with us we ascribe to his liver. With the gradual progress of

anatomy, however, these errors slowly passed away, and the brain came ultimately to be looked upon as the seat of intellect, the centre of sensation, and the source of motion.

When they had confined these functions to the nervous system, philosophers, and with them physicians, who were oftentimes philosophers, propounded the inevitable question, How does the brain exercise its activity? In what manner and by what agency does it think, feel, remember, will, and initiate movement? This leads us to the consideration of a subject which has proved one of the greatest stumbling blocks in the path of progress, and which affords a striking example of the influence of that *a priori* speculative philosophy of which I have spoken. I mean the belief in animal spirits.

In one form or another the theory of animal spirits dominated and obstructed medical thought from Hippocrates to the beginning of the nineteenth century. It is popularly ascribed to Descartes, but its roots reach back to antiquity. Appearing first in ancient medicine as the doctrine of Pneuma—that is, an ethereal principle by means of which the mind performs all the functions of the body—it became the innate heat of Aretæus, and with some modification the Archæus of Helmont and the sensitive soul of Stahl, until finally it survived in a somewhat questionable shape as the *vis medicatrix naturæ* of the school of Cullen. It represented under its various metamorphoses the vitalistic theory of nervous phenomena which has been so energetically opposed by the biochemical explanations of our own day.

The animal spirits were assumed to be a very fine and subtile ethereal fluid elaborated in the brain and used by the soul in the performance of its functions. "Not," observes Galen, "that this animal spirit is of the substance of the soul, but its prime agent while inhabiting the brain." On this point the observations of Dr. Bostock in his *Physiology* are interesting. He says the principal ground for the belief in the existence of animal spirits "seems to have been the idea that the brain is a secretory organ—an idea which was suggested by the great quantity of blood sent to it and by some supposed resemblance in its structure to other secreting glands. Yet as nothing cognizable by the senses is produced by it, it was concluded that it must secrete something of a subtile or ethereal nature peculiarly suited to the performance of the functions which belong to the brain, and which are so unlike those of other material substances. The idea seems to have been originally derived from the alchemists, and, after being incorporated with the metaphysics of the age, gave rise to a long train of mysticism." So firmly was the belief in animal spirits implanted in the minds even of scientific men that John Augustus Unzer, in the latter years of the eighteenth century, writes in his *Principles of Physiology*: "All the phenomena of motion and sensation manifested through the nerves render probable the existence of a remarkably subtile fluid essence which is

present invisibly in the medulla of the brain and nerves, and is the means whereby all the functions of both are performed. It is termed the vital spirit or nervous fluid, but it is not known how and when it contributes to the animal actions." And as late as the first quarter of the nineteenth century we find John Mason Good telling us in his *Study of Medicine* that the brain is a gland producing an ethereal fluid. "As we are justified," he observes, "by all the force of analogy in regarding it (the brain) as a gland, though unquestionably a gland of a peculiar kind, and as we are equally justified on the same ground of analogy in regarding the nervous power or energy by which it maintains a communication with every part of the system as a fluid of a peculiar kind, we are almost driven to the necessity of contemplating it as the source from which this fluid issues and by which it is supplied as it becomes exhausted." Such was the teaching of authority during centuries concerning the brain. Analogy, nothing more, was the slender foundation upon which men reared the superstructure of nervous physiology. The brain was a gland, as even the great Cullen and Malpighi believed; therefore, it must secrete. What? The answer was immediate—animal spirits—about the existence of which the majority of men had no doubt, and about whose nature and activity they talked as glibly as though they had been seen and weighed and measured.

With this explanation of mental life they were content, and so, wrapped about with mists of their own making, they stood still on the road that leads to knowledge; and they advanced, as we shall find, only when the animal spirits had been banished from the high places in nervous physiology.

Erasistratus, Herophilus, Galen, and others of the ancient writers believed in the division of the nerves into those of sensation and those of motion; but it is in the works of Aretæus the Cappadocian, who lived probably in the middle of the second Christian century, that we first find mention of the effect of the position of the lesion upon motion. Treating of paralysis, he observes: "If, therefore, the commencement of the affection be below the head, such as the membranes of the spinal marrow, the parts which are homonymous and connected with it are paralyzed, the right on the right side and the left on the left side; but if the head be primarily affected on the right side the left side of the body will be paralyzed, and the right if on the left side. The cause of this is the interchange in the origins of the nerves, for they do not pass along the same side until their terminations, but each of them passes over to the other side from that of its origin, decussating each other in the form of the letter 'X.'" This, so far as I know, is the first mention in medical literature of the fact that cord lesions affect motion on the same side, while brain lesions produce their symptoms upon the opposite side of the body.

Following Aretæus, cases were recorded by Valsalva, Wepfer, and Morgagni, in which paralysis upon one side of the body was

proven by autopsy to have been due to disease upon the opposite side of the brain, most commonly in the region of the great basal ganglia.

A quaint piece of writing upon this subject has been pointed out to me by Dr. Joseph Sailer, and is to be found in the preface to the edition of *Poor Richard's Almanac* for 1740. The spirit of a rival editor—Leeds—thus describes how he impelled Franklin to write a letter to himself: "Finding you asleep I entered your left nostril, ascended into your brain, found out where the ends of those nerves were fastened that move your right hand and fingers, by the help of which I am now writing unknown to you." It will be observed, he says, he entered the "left nostril," which would lead us to believe that the fact of motor decussation was current knowledge in those days, and that Franklin obtained it from some popular work on physiology. But concerning his idea that the nerves of the hand and fingers terminated in the brain and that the impulse to movement originated in these terminations, I am unable to form any definite conclusion. The eighteenth century physiology certainly taught no specific localization, and Franklin's statement is probably a shrewd guess founded upon the general belief as expressed by Boerhaave, that the nerves run without interruption from the periphery to the brain, and that voluntary motion had its origin somewhere in the cerebrum.

We have seen that the belief in motor decussation was prevalent from the time of Aretæus, but to Gall and Spurzheim must be attributed the credit of the first anatomical demonstration of the crossing of nerve fibres, which takes place in the pyramids. The knowledge of decussation led, however, to no more refined localization of function than that expressed by Haller in his great work, *Elementa Physiologiæ*, published in 1757. There he recognizes in a general way that if the brain be compressed that part of the body is deprived of motion the nerves of which arise from the compressed portion, and this represents the sum of topographical diagnosis until well along in the nineteenth century. As late as 1869 Niemeyer was obliged to say in his text-book: "It is rarely possible to recognize the seat and size of a tumor exactly, but it may be approximately decided in what part it is located, whether in the cerebrum, medulla oblongata, or cerebellum, at the base or convexity. The brilliant diagnoses where the precise localization of a tumor is fully confirmed by autopsy are not usually due to acumen in the observer, but are cases of lucky diagnosis."

I cannot leave this part of my subject without referring to a remarkable conjecture of Nicolaus Stenson, quoted by Sir Michael Foster. Writing in the seventeenth century on the "Anatomy of the Brain," Stenson expresses himself in these words: "If, indeed, the white substance (of the brain) of which I am speaking be, as in most places it seems to be, wholly fibrous in nature, we must neces-

sarily admit that the arrangement of its fibres is made according to some definite pattern, on which, doubtless, depends the diversity of sensations and movements." Here we have a suggestion which, had it been acted upon, would have gone far toward unravelling the truth, but it fell upon ears incapable as yet of understanding it, and so it remained barren of any fruitful consequences.

I wish now to return to the early views concerning the localization of the higher functions of the mind, and I cannot do better than begin with a quotation from the great Frenchman, Trousseau. He says: "You know, gentlemen, that medicine always takes its inspiration from the reigning philosophy, which means that every philosophical doctrine has in the history of medicine a corresponding medical doctrine." If we bear this important truth in mind we will many times discover that the explanation of some otherwise vague medical belief is to be found in the philosophy which underlies it. "The philosopher," says Aristotle, "should end with medicine, the physician commence with philosophy." And as medical thought to-day is prone to follow the naturalistic philosophy of Condillac, Bain and Spencer, just so the older physicians incorporated the fashionable philosophy of the times in their explanations of mental life. Plutarch and Theophrastus tell us of the physician Alcmaeon, believed to have been a contemporary of Pythagoras, who regarded the brain as the common meeting place of the senses. Hippocrates placed the mental faculties in the brain, and in treating of insanity he remarks that a man is sane if his mind is undisturbed. Plato taught that the mind has three distinct faculties, each possessing its separate seat: one, the concupiscent, having its seat in the liver; the second, the irascible, with its seat in the heart; the third, the rational, residing in the brain. He was followed in the course of time by Galen, Vesalius, and others, who, deriving their inspiration from his philosophy, acknowledged three spirits: the natural, passing from the liver with the blood; the vital, flowing from the heart to the body through the arteries, and the animal, distributed from the brain through the nerves. Curiously enough, Aristotle, although the disciple of Plato and the son of a physician, thought the brain a cold and bloodless organ whose function was to cool the ardent heat of the heart, which he regarded as the seat of life, and whence he believed all the nerves to arise. Galen, who exercised a greater influence over medical thought than any other man before or since, opposed the views of Aristotle, and taught that the brain was the organ of mind as well as the centre for all the senses and the source of motion. After Galen, according to Prochraska, the Arabians localized function in the different portions of the brain. One anterior ventricle was supposed to be the seat of common sensation, the other of imagination. In the third ventricle they placed understanding, and in the fourth memory. This was the doctrine of Duns Scotus and of Thomas of Aquin, in

his treatise *On the Powers of the Soul.* It was the classical teaching during the middle ages and early modern times, and is well expressed by Burton in that most curious of books, *The Anatomy of Melancholy.* "This forepart" (of the brain), he says, "hath many concavities distinguished by certain ventricles which are the receptacles of the spirits brought hither by the arteries from the heart, and are there refined to a more heavenly nature to perform the actions of the soul. Of these ventricles there are three—right, left, and middle. The right and left answer to their sight and beget animal spirits; if they be in any way hurt, sense and motion ceaseth. These ventricles, moreover, are held to be the seat of the common sense. The middle ventricle is a common concourse and concavity of them both; in this they place imagination and cogitation, and so the three ventricles of the forepart of the brain are used. The fourth creek behind the head is common to the cerebel or little brain and marrow of the backbone, the last and most solid of all the rest, which receives the animal spirits from the other ventricles and conveys them to the marrow of the back, and is the place where they say the memory is seated." From the foregoing quotation we may well understand what haziness characterized the views of our forefathers. It is true that Vesalius had called such beliefs "reckless opinions," "figments imagined, surely not without grave impiety," but the mind of Vesalius in this, as in so many other things, was far in advance of his age, and the reckless opinions, modified in various ways to suit their fancy or philosophy by Descartes and Willis, continued to rule men's minds to the end of the eighteenth and, indeed, strange as it may seem, found adherents in the early years of the nineteenth century.

As far back as the end of the sixteenth and beginning of the seventeenth century there had been opposition to the view that the ventricles are the manufactory and storehouse of the animal spirits. By the teachings and influence of Caspar Bauhin, Varolius, Spigelius, Hoffman, Caldani, and others the animal spirits together with the higher faculties, such as memory, imagination, and perception, were removed from the ventricles and placed in the solid matter of the brain, while some went so far as to assert that the intellectual functions were entirely independent of the brain and belonged to the immaterial spiritual soul. As men became emancipated from psychological mysticism, and as the new sciences of physics and chemistry came to exert a powerful influence upon thought, the tyranny of the animal spirits was slowly though surely undermined until at last they were dethroned altogether.

In 1784 we find Prochraska writing with a wholly modern tone in his *Dissertation on the Functions of the Nervous System:* "Notwithstanding the authority of these great names (Haller, etc.), the love of truth excited distinguished men, who advanced doubts as to this hypothesis of the animal spirits, and who showed that the argu-

ments adduced in its favor proved nothing when carefully analyzed, and that the whole hypothesis was altogether devoid of truth." He then goes on to say: "We will term the cause latent in the pulp of the nerves, producing its effect and not as yet ascertained, the *vis nervosa;* we will arrange its observed effects, which are the functions of the nervous system, and discover its laws." Here, then, we witness the exit of the animal spirits, which for centuries had held physiology so firmly in their grasp and had so effectually throttled every sort of progress. We have exchanged the transcendental speculations of metaphysics for the demonstrations of physics, and we shall shortly observe the good effects resulting from this removal of the physiological rubbish of antiquity and the placing of physiology upon an assured foundation.

The opinion long prevailed, as we have seen, that certain portions of the brain were connected with definite functions, some with organs of sense and voluntary motion, others with different vital functions. Among the first to point this out definitely was Willis, whose opinion was embraced and zealously defended by the celebrated Boerhaave and many of his disciples. The belief was derived partly from observations and experiments on the effects of injuries to the cerebral hemispheres, and partly from the investigations of comparative anatomy. Prochraska says very definitely, despite the teaching of Haller to the contrary, that it is "by no means improbable that each division of the intellect has its allotted organ in the brain," though he further observes that notwithstanding the labors of many eminent investigators the whole subject was still in obscurity.

The first systematic attempt, however, to localize cerebral function was made during the first quarter of the nineteenth century by the physician, Franz Joseph Gall, and his pupil, Johann Gaspar Spurzheim. The ill-repute into which their system has justly fallen has detracted from their real merit as scientific investigators. As a matter of fact, they were among the most eminent men of their time, their contributions to anatomy are valuable, and it was Gall who, by dissecting the brain-stem from below upward, inaugurated the method which was subsequently to produce such notable results.

These two physicians elaborated a "physiognomical system" which, under the name of phrenology, attracted a larger share of attention than its real merits justified. Gall divided the skull into twenty-six and Spurzheim into thirty-five regions, each supposed to represent the organ of some particular mental aptitude.

While it is now universally recognized that at the time of its promulgation phrenology was premature, being incorrect both in localization and in the psychological analysis of the mind, still it had the great merit of provoking severe criticism, which was, unfortunately, often extremely personal, and thus of drawing attention to the whole subject. Although discredited itself, one of its important

results was that from the time of Gall and Spurzheim the tendency has always been more strongly toward a topographical localization of mental activity.

I have mentioned as one of the causes contributing to the backward state of neurological knowledge the absence of an adequate scientific method. Until the introduction of the inductive method as propounded by Bacon and further elaborated by Newton, Locke, and later by Hume and John Stuart Mill, there was no possibility of verifying and controlling hypothesis by fact, and, especially in the domain of the nervous system, no means of advancing from the known to the unknown. But with the advent of physiological experimentation the aspect of things was changed. The illustrious Haller was among the first of physiologists to employ this method in his work. "As the nature of the brain and of the nerves is one and the same," he says, "so are these alike in function. In treating of them we will so far as possible make use of experiments, nor will we at first at least go beyond the testimony of our senses." And if we wish to observe what a revolution the new method wrought we have only to compare the mystic Swedenborg's *Œconomia Regni Animalis*, published in the middle of the eighteenth century with Haller's *Elementa Physiologiæ*, published a few years later. By means of experiment, first, Magendie, in 1822, and later Sir Charles Bell discovered that the anterior spinal roots are motor and the posterior sensory in function, thus beginning a new era in nervous physiology and laying the foundation of the subsequent progress, which has continued without pause to our own day.

In the reaction following the teaching of Gall and Spurzheim, whose conclusions went far beyond the facts, the pendulum had swung to the opposite extreme, and from the experiments of Magendie, Longet, and in particular of Flourens, special localization of function in the cortex was discarded and the classical physiology taught, even against the strongest evidence to the contrary, the equivalence of mental function, that is, the brain as a whole, not any definite portion, was considered to be the physical substratum of mental activity.

The work of Flourens corroborated the previous experiments of Molinelli, Rolando, Krauss, Hertwig, and others, and was itself corroborated by the later researches of Serres and Desmoulins. The theory received the sanction of the celebrated Cuvier, and so convincing apparently was the evidence upon which it was founded that it formed the belief of the ablest physiologists down to the present period, which began in reality in 1822, but which attained no special influence until 1861.

But before considering the question of aphasia I wish to preface a word concerning the anatomy of the cerebral convolutions. The earlier physicians were surprisingly ignorant of the anatomy of the

hemispheres, and in this connection there is an interesting paragraph in the work on *Apoplexy* and *Lethargy*, written by the celebrated Cheyne, of Edinburgh, and published in 1812. "Our knowledge of the brain," he observes, "is still circumscribed within very narrow bounds; we do not know with certainty anything beyond the form, consistence, and color of its various eminences, depressions, and cavities, and the origins of the nerves and distribution of the bloodvessels which connect this organ with the rest of the system. We, indeed, know from the effects of similar diseases of the brain that sensation and volition are functions of this organ, but we are as much in the dark with regard to the use of most of its parts, its ultimate structure, and the kind of influence which it exerts over the body and most of the circumstances upon which the origin and transmission of that influence depend as we are with respect to the nature of the impressions made by external objects upon our organs of sense, or the sensations associated with those impressions." A part of the ignorance of which Cheyne speaks was certainly due to the beliefs in vogue concerning the cerebral convolutions. Their arrangement was thought to be purely a matter of chance, and in the older records of cases of brain disease we usually find the position of the lesion roughly described as being in the anterior, middle, or posterior lobe. It remained for Leuret and Gratiolet to demonstrate clearly that there was an orderly plan in the convolutions, which could be traced from the inferior mammals, through the monkey up to man. The researches of these great observers, and especially of their successors, Ecker, Broca, and Gromier, by mapping out for us the morphology of the external surface of the brain, removed the chief anatomical obstacle that I have mentioned, and made it possible for us to describe accurately the precise location of any lesion. The scholarly little work of Ecker on *The Convolutions of the Human Brain* and that of Gromier entitled a *Study upon Cerebral Convolutions in Man and Monkey* did much to lead men out of the labyrinth of error, where it was customary "to regard the convolutions as a series of folds without order or arrangement, and draughtsmen represented them much as they would a dishful of macaroni."

It is commonly stated that the first case in which the loss of articulate speech was attributed to a lesion in the left frontal lobe was reported by Thomas Hood in 1822. This, however, is not historically accurate. There is a case detailed by Pourfour Petit in 1766 which represents probably the first case in medical literature. It is recorded by Austin Flint in his *Physiology of Man*, from which I have taken it. Writing in his *Nouveau système du cerveau* Petit says: "Some time after I had made the experiments which I have just reported a cavalryman of the garrison, aged thirty-five years, was brought into our hospital. He had been seized the day before

with paralysis of the entire right side, which had occurred after a slight pleurisy, from which he had recovered. He could move neither the arm nor the right leg, nor could he maintain himself in his seat. The lower jaw was not distorted. He opened and closed the mouth with facility. He could move the tongue only with great difficulty, and could not protrude it from the mouth, nor pronounce any word. He retained sensation on the paralyzed side. A month after he had entered the hospital he moved the tongue pretty easily, and even protruded it a little from the mouth, but he could pronounce nothing but "Non." After death I removed the brain and spinal cord. I began by dissecting the spinal cord, in which I found nothing abnormal, nor in the right side of the brain. But I found on the left side the entire anterior protuberance which contains the internal and superior corpora striata, the middle and the external or inferior, dissolved and converted into a substance resembling the lees of wine. It did not appear that this part had been swollen and that it had become larger than natural. Neither the optic thalami nor the optic nerves were injured."

From this most interesting case of Petit nothing was written concerning aphasia until 1822, when the English physician, Thomas Hood, recognized that disturbance of speech was caused by a lesion affecting the frontal lobes of the brain. In 1825 Bouillaud, in France, as the result of experimentation and clinical experience, maintained that a lesion in the anterior lobes causes loss of speech, and he further believed in the existence of cerebral motor centres, destruction of which causes localized paralysis. In a paper read before the Medical Congress at Montpellier in 1836 Marc Dax reported impairment or loss of speech in 140 cases of right hemiplegia, from which he concluded that the faculty of articulate language is situated in the left anterior lobe. However important were these observations in pointing the way, it is to Paul Broca that we owe the definite localization of the speech centre. In 1861 Broca, as the result of clinical observation, placed it in the third left frontal convolution, and in the heated discussion on aphasia at the Academy of Medicine at Paris, in 1864, further light was thrown upon the subject, the conclusions of Broca were confirmed, and thus, after the lapse of centuries, we behold the first absolutely definite localization of function in the cerebral cortex. Following Broca's dramatic and truly epoch-making discovery, came the observations of Hughlings Jackson on localized epileptiform convulsions, those of Aubertin, Charcot, Pitres, Falret, Trousseau, Séguin, Bastian, Broadbent, Wernicke, Kussmaul, Fritsch and Hitzig, and a host of others whose labors have pointed the way from haziness to definite scientific conceptions. They are the pioneers who have laid the foundations of neurology broad and sure. And, based largely upon their labors, neurology has gone forward, often it is true, with halting

steps, but none the less forward, until to-day it possesses a body of assured truth upon which we daily levy tribute in our battle with disease.

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REVIEWS.

SUBJECTIVE SENSATIONS OF SIGHT AND SOUND, ABIOTROPHY, AND OTHER LECTURES. By SIR WILLIAM R. GOWERS, M.D., F.R.C.P., F.R.S. Philadelphia: P. Blakiston's Son & Co., 1904.

THIS compact volume of 250 pages is a presentation in lecture form of a variety of subjects mainly pertaining to neurology. The first of the articles, that on subjective visual sensations, an address to the Ophthalmological Society of London, is an excellent presentation of various visual phenomena seldom written of and little understood. In explaining the relation of the visual sensations to the functions of the cerebral cortex he invokes the aid of the visual disturbances of hysteria, reversing his own previous attitude, and places the subject in such a state that a careful neurologist or ophthalmologist will find no little intellectual exercise in straightening out the tangle of argument. The study of color-vision and the visual fields, the subjective visual sensations of migraine and epilepsy, all of which are used in his explanation of the relation of peripheral and central vision, are, apart from this, valuable contributions to the subject and interesting reading.

Subjective sensations of sound are treated in a similar, if less complex, way.

The need for a comprehensive term to designate a large group of diseases affecting the nervous and muscular systems dependent on an inherent lack of vitality, or working ability, has long been felt. In the third lecture Gowers proposes the term "abiotrophy" to supply this want, and the term has obtained general use among neurologists in a very short time. The adjective abiotic, while strictly correct, is somewhat foreign in sound to abiotrophy, and a tendency has been manifested to use the term "abiotrophic" in its place in case-records, etc. The explanation and discussion of various forms of abiotrophy—the muscular dystrophies, etc.—is presented in the following lectures.

The effects of lead and arsenic on the nervous system are considered in separate lectures. In the remaining lectures syphilis of the nervous system, syringomyelia, and the use of drugs are treated. All of the articles are valuable contributions to their respective subjects. Gowers has set an example for those of wide experience and sane judgment in correlating isolated facts and

sifting the evidence concerning various subjects and presenting them in book form in an authoritative way. As parts of a book the individual articles have an added value on account of their permanency, and because the author—than whom there is no better judge of what is of value in neurological literature—considers them worthy of being so placed. D. J. McC.

THE THERAPEUTICS OF MINERAL SPRINGS AND CLIMATES. By I. BURNEY YEO, M.D., F.R.C.P., Emeritus Professor of Medicine in King's College, London; Consulting Physician to King's College Hospital, etc. Pp. 760. Chicago: W. T. Keener & Co., 1904.

WE welcome this volume, which suggests the author's *Climate and Health Resorts* as its foundation, but which, based upon a larger and riper experience, brings us to the present. With the increased attention of late given to physical measures for the restoration of health comes added interest in the subject, so that this book is timely and important. With the knowledge shown in other works, this broader view cannot but be of advantage to the reader. Of the first part—mineral springs—much has been written from the viewpoint of this exploitation, through an effort to obtain a scientific explanation of varying therapeutic effects when chemical analysis shows minute differences in constitution, to serious attempts to place a fair statement as to what conditions, and more particularly, what patients are likely to be benefited. From the patient's standpoint this book has been written, even if the difficulties of the "indifferent springs" have not been fully elucidated. Of the topics presented, the nature, composition, and classification of the springs, modes of application, action, accessory method, lead to the description of the principal springs, which are considered alphabetically. The application of mineral water and baths complete the subject. If criticism of an excellent book be not unkind we would suggest that, in addition to those considered, there are some which have been omitted, and that perspective as shown in the use of smaller type is not always in accord with importance. As to the second part—Climate and Climatic Resorts—the divisions embrace climate and climates, sea or mountain, seaside and mountain resorts, winter quarters, the Western Riviera, sea voyages, and, finally, the practical portion —the application and selection of climates and treatment in sanatoria, which includes a list of the same. The places mentioned are such as, in the judgment of the writer, "are fairly accessible to and likely to be visited by English invalids." Here, again, we except to the author's limitation of the globe-trotting propen-

sities of our English cousins, and believe that many places not here mentioned have a climate, not weather, of which he might hear somewhat favorably from his professional brethren. Not that we believe that what our country possesses needs consideration, much less eulogy, but now that our own authors have presented volumes of no mean reputation, a complete guide cannot be predicated unless these volumes have been consulted. To be sure, we find mentioned many resorts of household reputation, but too briefly for accurate judgment as to their value. As a book for consultation, if not so complete, yet more readable than an assemblage of official reports with which we are familiar, as a fair statement of well-ascertained facts, as a book of attractive presentation, bearing the impress of the author's personality, we give this a prominent place in our library.

R. W. W.

A Practical Treatise on Nervous Diseases for the Medical Student and General Practitioner. By F. Savary Pearce, M.D. New York and London: D. Appleton & Co., 1904.

Both Gowers and Oppenheim have well demonstrated that it is not at all necessary to differentiate the student or general practitioner from the skilled neurologist in presenting the subject under consideration. With such standards of excellence in book writing, the assertion in the title of a new work that it is primarily intended for the student and general practitioner should not protect it from criticism or from comparison with what is best in neurological literature. Were the book intended for the students of the institution of which the author was professor of neurology it would undoubtedly fill a distinct want, were it followed in preventing a confusion of such ideas as are frequently presented with that of established teaching. Beyond such a scope of influence, in the hands of the general practitioner, it would do harm as an inaccurate presentation of an important subject. To teach that "paresis" of the third nerve produces nystagmus, protrusion of the eyeball, and ptosis" is, to say the least of it, misleading. Many such misstatements might be quoted.

The general arrangement of the subject-matter and its form of presentation is good; the English is, however, complex, compressed, and very often with difficulty understood.

The real value of the work lies in the large number of well-executed illustrations, which are, on the whole, appropriate and pertinent to the subjects illustrated, and are here permanently placed on record as a real addition to the subject of neurology.

The book cannot be recommended to the student or the general practitioner, for whom it was intended, but should be in the hands

of every specialist of the subject—every specialist who has written or intends writing a book. To such it will have a peculiar and personal value. M.

ATLAS AND EPITOME OF OPERATIVE GYNECOLOGY. By DR. OSKAR SCHAEFFER. Edited by J. CLARENCE WEBSTER, M.D. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

As stated by the author in his preface, the difficulties of demonstrating the various operations of gynecology, particularly the different modes of attack by the vaginal route, are probably greater than in any other province of surgery. To meet this difficulty is the object of the present volume. When one considers the inherent difficulties of the attempt only praise can be felt for the way in which the artist has fulfilled his part.

As to the gynecological teaching, there is much that might be criticised, as, for instance, the recommendation of Hegar's perineorrhaphy, the including of hysterocleisis, and colpocleisis and the vaginal fixation of the uterus. We believe that the book will, however, if used as intended by the author, in conjunction with a good clinical course, serve a useful purpose. W. R. N.

DISEASES OF THE NERVOUS SYSTEM: A TEXT-BOOK FOR STUDENTS AND PRACTITIONERS. By H. OPPENHEIM, M.D. Translated and edited by EDWARD E. MOYER, A.M., M.D. Second American edition. Philadelphia: J. B. Lippincott Co., 1904.

THIS new edition of the most popular of the German text-books follows close on the third German edition. The plan of the German edition is closely followed, and additions are made only when it is necessary to elucidate some obscure point or to give credit to American investigators. For clearness of conception, consideration of material, scientific accuracy, and thorough treatment, the German edition finds no equal, either in nervous diseases or other fields of medicine. The book has lost none of these qualities in the translation, but in an attempt at a literal translation of the German text the English construction is frequently awkward and clumsy. There is little excuse for this, as our own language is much better adapted for purposes of condensation of material than is the German. The improvement over the preceding edition is evident in the number of illustrations of disease types and of pathological specimens. There is no other work so well illustrated, nor is there any to which the illustrations are of so much value in elucidating

the text. They impress one as an essential element of the work, and not merely, as is so often the case, as added pictures to attract the eye.

Much has been added to the treatment of the functional nervous disorders, but not from an American standpoint. Fifteen pages of treatment are given for neurasthenia and hysteria, with the Weir Mitchell rest treatment relegated to a small paragraph of fine print of less than one-fourth of a page.

To those who are unable to read the original German edition the English translation can be recommended as one of the best text-books on the subject. D. J. McC.

LES MALADIES DE L'ESTOMAC. Paris: J. Rueff, Editeur, 1904.

THIS royal octavo of about 1200 pages presents, in addition to the clinical experience and therapeutic teaching of the author for fourteen years past at the "Hôpital de la Petit," an admirable and exhaustive review of the work of the leading specialists in this field throughout the world. Briefly stated, the book is divided into five parts, viz.: first, clinical and physical examination of the stomach and contents; second, dyspepsias, general considerations, treatment, nosology, prophylaxis, symptomatology; nervous, alimentary, and reflex types and the treatment thereof; changes in urine and blood occurring therein; pyloric stenoses, gastric fermentations, hydrotherapy; third, organic maladies of the stomach, etiology, pathology, and treatment; fourth, pathogenic role of stomach affections in relation to other organs and their functions; fifth, the reaction of other maladies on the stomach. This work is thorough, and presents the views of the leading authorities and specialists throughout the world, the German authorities, as usual, leading in the number of references, although French and American authors are quite copiously quoted. All in all, this volume will compare very favorably if, indeed, it will not surpass, any similar work issued to date. E. A. H.

VAGINAL TUMORS, WITH SPECIAL REFERENCE TO CANCER AND SARCOMA. By W. ROGER WILLIAMS. London: John Bell, Sons & Danielsson, 1904.

THIS very valuable book, small in size, but covering its ground very fully, is to be recommended to all who are interested in neoplastic vaginal formations. While the subjects considered are not among the most frequent to be met with in a medical practice, yet

the great importance which they assume is sufficient excuse for the appearance of this admirable volume.

While the scientific side of the question, namely, the etiology of the genesis of these formations, is not slighted, the book is replete with the practical details and, as the author claims in his preface, has the great recommendation of conciseness. There are five chapters, the first two being devoted to cancer and sarcoma; the third and fourth to non-malignant growths, as myoma, neuroma, etc., while the last deals with the very interesting cystic formations.

W. R. N.

PORTFOLIO OF DERMOCHROMES. By PROFESSOR JACOBI, of Freiburg, in Breisgau. English adaptation of text by J. J. PRINGLE, M.B., F.R.C.P., Physician to the Department for Diseases of the Skin at the Middlesex Hospital, London. Vol. II. New York: Rebman & Co., 1903.

THE high standard of excellence reached in the first volume of Jacobi's *Atlas of Diseases of the Skin* is well maintained in the second and concluding one. Many of the portraits leave little to be desired in the way of accurate and lifelike representations of diseases of the skin.

This volume of the *Atlas* contains forty-four plates, of which fifteen are devoted to cutaneous syphilis. We note with hearty approval that the author has thought worth while to give some space to the subject of drug eruptions—an important subject from many points of view to which not enough attention is paid. Six plates are given to the lesions which result from the internal use of the iodides, the bromides, antipyrin, arsenic, and copaiba. An especially interesting portrait is the one representing arsenical hyperkeratosis of the palm, not only because it is a truthful representation of this form of keratosis, but because of its importance as an occasional forerunner of epithelioma. The eleven portraits of the various forms of eczema are among the very best we have ever seen, the plate representing eczema madidans being wonderfully lifelike.

As in the first volume, the text is extremely condensed, being limited to the briefest consideration of the etiology, diagnosis, prognosis, and treatment of the diseases illustrated. In the endeavor to be brief matters of some importance are occasionally overlooked, as when no mention is made of the fact that pemphigus neonatorum is almost certainly identical with impetigo contagiosa, and may prove fatal in very young infants.

In conclusion, we have no hesitation in saying we believe this to be one of the very best atlases of diseases of the skin yet published.

M. B. H.

THE EYE, ITS REFRACTION AND DISEASES: THE REFRACTION AND FUNCTIONAL TESTING OF THE EYE, COMPLETE IN ITSELF. In twenty-eight chapters, with numerous explanatory cuts and diagrams. By EDWARD E. GIBBONS, M.D., Assistant Surgeon to the Presbyterian Eye, Ear, and Throat Hospital; Demonstrator and Chief of Clinic of Eye and Ear Diseases in the University of Maryland, Baltimore. New York and London: The Macmillan Co., Ltd., 1904.

THE beginnings of the chapters of this book open up an attractive outlook. Certain subjects are here brought together not accessible, as a rule, in the ordinary text-books. The writer makes free use of elementary formulæ in his treatment of ophthalmic optics. We regret to have to note a number of inaccuracies which are likely to prove stumbling blocks to the student. The printer's part in the work is most excellent, and will no doubt prove a valuable adjunct in the sale of the book. T. B. S.

PHYSICAL TRAINING FOR WOMEN BY JAPANESE METHODS (JIU-JITSU). By H. IRVING HANCOCK. New York and London: "The Knickerbocker Press," G. P. Putnam's Sons, 1904.

JIU-JITSU gives the average American woman an entirely new view of her Japanese sister—it seems almost impossible to believe that they are so much in advance of a race of women to whom systematic exercise is a threadworn subject.

The author has illustrated his book profusely, and the text is most concise, but the great drawback to the practicability of the method is the fact that it requires two persons to carry out most of the exercises. The exercises for developing the "chest and the hollow between the shoulders" are particularly good, and can be done by any woman at home. The chapters on "Our Outdoor Sports for Women" and "Sleep and Its Value" are full of suggestions that are worthy of a trial at least. Some attention has been given to "obesity and leanness," but nothing particularly new is advised.

On the whole, the book is very interesting, and the methods carried out in a regularly organized class would undoubtedly prove of great value to the students, but as a guide for the individual it is of little use, as only two or three of the exercises can be done alone; there must be an "assailant" and a "victim" to carry out the methods of "jiu-jitsu" successfully. W. R. N.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Primary Endothelioma of the Pleura.—PAUL BONHEIM (*Münch. med. Wochenschr.*, 1904, li. p. 741) reports three cases of primary endothelioma of the pleura, and discusses the diagnosis and pathology. The first case, a man, aged fifty years, was treated for three months for left-sided pleural effusion, a clear serous fluid being obtained by puncture. A month later a litre of clear fluid was again withdrawn. After a week he re-entered the hospital on account of dyspnœa and continuous pain in the side. He was much emaciated; hæmoglobin, 60 per cent. The left side showed evident signs of fluid, but the lower costal spaces of the lateral chest wall were shrunken. The first aspiration again yielded clear, serous fluid, but the second was markedly hemorrhagic. The patient suffered most intense pain in the side, controlled only by morphine. Death occurred suddenly six months after the beginning of treatment. The anatomical diagnosis was right-sided adhesive pleurisy; hemorrhagic exudate on the left, the pleura being covered with a thick fibroid exudate; compression and chronic pneumonia of the left lung; embolism of right pulmonary artery. Microscopically, sections of the pleura showed a dense network of connective-tissue fibrils with few spindle-shaped nuclei, and scattered through this groundwork numerous anastomosing, long, round tubules lined with cubical epithelial cells, in places arranged in several layers. The deeper layer of the exudate was composed of a less cellular connective tissue with round-cell infiltration and only an occasional tubule.

The second case, a man, aged fifty-five years, complained of pain in left side and dyspnœa. There were evident signs of fluid in the left pleural cavity, and clear serum was obtained on puncture. He was tapped in all six times, the fluid after the first puncture being markedly hemorrhagic. The chest was aspirated on account of the rapid return of the fluid and of the dyspnœa, and two ribs were finally resected a

month after entry. The pleura was thickened and covered with small prominent, shining nodules, which were regarded as tubercles. The microscopic report, however, showed an excised piece to consist of an intercommunicating system of tubules lined with low epithelioid cells. The patient died three and one-half months after the operation. The autopsy showed endothelioma of left pleura, with metastases in the lungs, glands, spleen, liver, and adrenals.

The third case was that of a Chinaman, aged thirty years, who was admitted with symptoms of a severe left-sided exudative pleurisy, and rapidly died of cardiac weakness. The condition of the pleura was found to be the same as in the other cases.

All cases reported in literature have presented a microscopic picture similar to that observed in these three instances. Macroscopically, two forms may be distinguished: 1. A diffuse, uniform thickening resembling, even at autopsy, an ordinary fibroid pleurisy as in Case I. 2. More commonly the thickened pleura is studded with small cartilaginoid projections.

Cases of pleural endothelioma run their course under the picture of hemorrhagic pleuritis, but there are certain symptoms which should direct attention to the condition. The diagnosis has been made *intra vitam*. A clear, serous fluid on the first tapping, becoming blood-tinged later, and then more and more hemorrhagic until it has a deep chocolate-color, is very suggestive. This condition has been noted in nearly all reported cases. The fluid reaccumulates rapidly, and, as Podack remarks, each successive puncture gives less and less relief. Finally, the heart becomes fixed in its displaced position and does not recede after the fluid has been withdrawn. Of course, the primary step is to exclude tuberculosis and secondary carcinoma. Podack demonstrated clumps of tumor cells in the exudate from his case, but this would be no constant finding. Fraenkel has pointed out as characteristic the retraction of the lower intercostal spaces in spite of the presence of a large amount of fluid, and Bonheim emphasizes the very evident progressive retraction of the whole side of the chest. This was strikingly present in the first case. The reported cases have been almost exclusively in males, and the left side has usually been affected. In regard to the pathology of these tumors, Benda was able to demonstrate their growth from the pleural endothelium, and Podack from the lymph spaces. Numerous names have been suggested for the condition: carcinoma, endothelial carcinoma, lymphangitis carcinomatodes, lymphangitis proliferans, alveolar endothelial sarcoma. Bonheim thinks the term endothelioma is preferable in that it conveys no false impression.

Blood-pressure Estimations in Arteriosclerosis.—KEIGI SAWADA (*Deutsche med. Wochenschr.*, 1904, p. 425). The maximum systolic pressure was taken with the Riva-Rocci instrument, as modified by v. Recklinghausen, a firm cuff 15 cm. wide being substituted for the original narrow one. The pressure readings were made after the patients had quietly rested for from a half to one hour in the polyclinic, and after lying down fifteen minutes with the arm band in position. Recklinghausen and Miller give the normal maximum systolic pressure at from 105 mm. to 115 mm. mercury. In a large number of readings Sawada found variations from 90 mm. to 120 mm. Pressure over

130 mm. he considers increased, from 120 mm. to 129 mm. not definitely increased, and below 120 mm. normal.

Of 98 cases of arteriosclerosis in which the heart and kidneys were apparently perfectly normal, in 83 the pressure was normal, in 5 increased, and in 10 not definitely increased. The highest pressure in any case was 176 mm. He divides these cases into three classes: (1) arteries just palpable; (2) arteries distinctly thickened, and (3) actual "goose-neck" arteries. Of 42 cases in the first class, 2 showed increased pressure and 3 pressure not definitely increased; of 42 in the second class, 2 showed increased pressure and 5 pressure not definitely increased; of 14 cases in the third class, 1 showed increased pressure and 2 pressure not definitely increased. The elevation in all but 1 case was slight, and, accepting with Hensen 20 mm. of mercury as the amount of pressure necessary to obliterate the rigid arterial wall alone, most of the figures would be reduced to high normals. Of 206 cases of arteriosclerosis examined, there were 24 with accentuated second aortic sound without any evidence of kidney disease—13 with normal pressure, 10 with increased pressure, and 1 border-line case. Sawada believes that the accentuation of the second sound must be due to factors other than simply increased pressure, as had been previously pointed out by Curschmann. Of 43 cases of arteriosclerosis associated with cardiac insufficiency, in 28 the pressure was normal, in 10 increased, in 5 not definitely increased. In 10 arteriosclerotics with small granular kidneys all showed a marked increase in tension, ranging from 150 mm. to 205 mm. In 4 cases it was over 180 mm. In cases of simple arteriosclerosis Sawada has never observed pressures over 170 mm., except in 1 doubtful case. In 22 further cases associated with albuminuria—excluding those which were recognized as interstitial nephritis—the pressure was normal in 15, increased in 3, not definitely increased in 4. The highest pressure was 148 mm.; 8 of his cases belong to the interesting group occurring, without apparent cause, in children and young adults from fourteen to twenty-six years of age. In 3 of these cases the pressure was over 120 mm., reaching in one 131 mm.

To summarize: 12.3 per cent. of the cases examined showed an increased blood pressure, usually within 130 mm. to 160 mm. Two-thirds of the cases with increased tension were associated with an accentuated second aortic tone. However, there was more frequently an accentuated second aortic without increase in tension. A constant blood pressure over 170 mm. suggests the existence of a chronic interstitial nephritis, even if albumin be absent from the urine.

The Significance of Traces of Blood in the Feces.—Dr. L. Joachim (*Berl. klin. Wochenschr.*, 1904, xli. 466). The chemical investigation of the feces to discover minute traces of blood has attracted considerable attention in the past few years as an aid in the diagnosis of certain diseases of the alimentary canal. Joachim has investigated the condition in a large number of patients to ascertain what reliable conclusions can be drawn from it. He has used both the guaiacum test of Weber and the aloin of Rossel. He finds the aloin test the more delicate of the two, but each has some advantage over the other, and he recommends using both in doubtful cases. In patients suffering with no disease that might explain the presence of blood in the stools the tests

were invariably negative, except in several instances in which they had eaten articles of food containing blood. After slight nose-bleed the tests were positive; after hæmoptysis usually negative, as little sputum is swallowed. In pneumonia blood was never found in the feces. In carcinoma of the stomach blood was missed in the feces in only a single instance out of nineteen. The amount of blood in most instances was very small, but it was constantly present—at least in no case was the stool free from blood for several successive days. Out of twenty-eight cases of gastric ulcer blood was discovered in the stools of twenty-three, not, however, constantly in small amounts, as in the case of carcinoma, but in relatively large quantities, varying with longer or shorter blood-free periods. The hemorrhages bore no apparent relation to the ingestion of solid food. In a large number of cases with tuberculous ulceration of the intestines blood was never demonstrated in the stools. Out of six cases of typhoid fever the tests were positive in two; in one of these the stools showed a positive reaction the day before the onset of a severe intestinal hemorrhage. Boas has observed such "premonitory" traces of blood in cases of gastric ulcer. In a case of mercurial poisoning the tests were constantly positive. They were uniformly negative in cases of gastric catarrh, gastroptosis, intestinal parasites—excepting one case of Balantidium coli—and in lesions of the neighborhood of the intestinal canal, as appendicitis, subphrenic abscess, etc. In cases of general passive congestion, as in broken cardiac compensation, blood was repeatedly found, while in a number of cases of cirrhosis of the liver with portal stasis it is remarkable to note that it was absent. In a case of catarrhal jaundice blood was unexpectedly found on several occasions at the height of the disease, while in several cases of cholelithiasis the tests were constantly negative. A carcinoma of the pancreas gave negative results; a hemorrhagic pancreatitis positive.

Joachim was able to demonstrate traces of blood in the stools of healthy persons after the ingestion of only 3 g. of blood. The chemical tests are much more delicate than the spectroscopic.

While this method of searching for minute quantities of blood in the stools may be very helpful in certain cases, the conditions which may lead to intestinal hemorrhage are so numerous that its value is greatly impaired. As sources of error the author mentions hemorrhoids, menstruation, hemorrhages from the gums and nose, hæmoptysis, and the ingestion of articles of food containing blood. Tests after eating well-cooked meat were negative.

The Value of Jousset's Inoskopy.—E. Körmöczi and K. Jassniger (*Deutsche med. Wochenschr.*, 1904, xxx. p. 342) say that, in order to discover the presence of a very small number of tubercle bacilli in a large amount of exudate, Jousset has introduced a method which he calls inoskopy, consisting in digesting with pepsin the coagulum which forms after the fluid has been allowed to stand, centrifugalizing the digested mass and examining the sediment. Using this method, he reports interesting and surprising results. In 17 cases of pleurisy with effusion, without apparent pulmonary lesions, he found tubercle bacilli in all. In 12 cases of ascites he demonstrated them in 3, although in none of these cases had the diagnosis of tuberculous peritonitis been made. In 2 cases of apparent typhoid fever Jousset established the diagnosis of acute miliary tuberculosis by obtaining tubercle bacilli from

the blood. In 10 cases of chronic pulmonary tuberculosis he found tubercle bacilli in the blood of 2, both complicated with renal tuberculosis, and describes a transient "bacillémie" associated with symptoms of a febrile gastric disturbance, the bacilli disappearing from the blood with the abatement of the symptoms. Following closely the description of the method as given by Jousset, Körmöczi and Jassniger obtained positive results in 3 out of 8 cases of pleuritic effusion. Two cases of ascites were negative, and the heart's blood obtained at autopsy from cases of acute miliary tuberculosis, positive once and doubtful once out of 4 cases. All of the cases examined were definitely tuberculous, and in view of so many negative results they believe that the value of Jousset's method has been overestimated. As possible sources of error they lay emphasis on small scratches on the slides which retain the fuchsin stain and easily deceive unless great caution is used. Small rents in the film and particles of the fuchsin stain which resist decolorization may present figures very similar to isolated tubercle bacilli. The most deceptive pictures occur in connection with the blood coagula, in which are always present masses of small red rods, shorter and thicker than the true tubercle bacilli. The more thoroughly the coagulum is washed the less numerous are these figures, which Körmöczi and Jassniger refer to crystalline particles of blood-coloring matter.

THERAPEUTICS.

UNDER THE CHARGE OF

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Mercurial Inunctions in Syphilis.—Dr. Gailleton describes the most approved form of this classical treatment thus: At each inunction from 1 to 1.5 drachms of mercurial ointment are used and rubbed well into the skin for ten minutes; then gauze or linen is laid over the part. The next morning the skin is bathed with water and a powder of equal parts of soap and sulphur. Each inunction should be made in a different place, the insides of the arms and thighs, the sides of the thorax and abdomen, the folds of the buttocks, the popliteal spaces, axillæ, the hairy region of the pubes, the palms and soles being successively used. The author advises one inunction daily for twenty days, a rest of four days, and a resumption every two days for ten to twenty days. The results achieved will show whether a second like series is necessary. The condition of the kidneys, of the digestive tract, and of the mouth must be carefully watched, the latter being frequently cleansed by antiseptic washes. Patients with irritable and tender skins often cannot endure this form of treatment. Inunctions are especially indicated in grave syphilis at all periods and in rebellious syphilides of the secondary tertiary stage. When mixed treatment is given, potassium iodide is prescribed in connection with the inunctions. The treatment by friction

is contraindicated in pustuloerosive syphilides and other conditions where there are raw surfaces giving an opportunity for absorption.—*Journal de médecine de Paris*, 1904, No. 15, p. 148.

Iodipin.—Dr. M. Fränkel states that this substance is a combination of iodine with oil of sesamum. It is furnished in two strengths of 10 per cent. and 25 per cent. of iodine, respectively. It is a clear, yellow, oily fluid, smelling and tasting like oil of sesamum. The author has used the 10 per cent. iodipin internally in cases of secondary and tertiary syphilis, and has never seen resulting symptoms of iodism, one patient in particular receiving during the course of four to five months over 60 ounces of the substance without untoward symptoms, and with the result of bettering his general condition and increasing his weight. Potassium iodide previously had caused coryza and acne. In chronic bronchitis with asthmatic attacks, the use of iodipin is recommended. Subcutaneous injections of the 25 per cent. strength, in doses of 0.5 ounce or more daily, achieve good results in tertiary syphilis and are attended by no symptoms of iodism. The author reports a case of beginning tabes dorsalis, in which the use of iodipin seemed to have caused a disappearance of the symptoms and to have stopped the progress of the disease. As an injection into syphilitic abscesses and broken-down gummata, iodipin is useful.—*Wiener klinische therapeutische Wochenschrift*, 1904, No. 15, p. 432.

Lumbar Puncture in Ear Lesions.—M. Lumineau has studied the effect of lumbar puncture in various aural disorders, such as affections of the labyrinth, otitic scleroses, dry and cicatricial otitis, and has concluded that aural vertigo, especially when accompanied by Ménière's syndrome, is the symptom most amenable to treatment by this means. Simple labyrinthitis receives the greatest benefit from this treatment, and no other means seems to relieve the condition as effectually. Labyrinthitis with vertigo, with subjective sounds, and the mental state which results from these is also modified by this treatment. The vertigo disappears, the mental condition becomes normal, and the auditory disturbances tend toward disappearance. These troubles are most likely to be ameliorated if they are sequelæ of old suppurative conditions. After dry otitis the results of puncture are less favorable. However, in all aural lesions where other treatment has proved ineffectual, lumbar puncture is worth trying and may be followed by success.—*Revue française de médecine et de chirurgie*, 1903, No. 6, p. 137.

Fersan.—Dr. B. Ehrmann makes the following report upon this preparation of iron and phosphorus. It is prepared from the blood of cattle, 1 per cent. salt solution, and concentrated hydrochloric acid, and when ready for administration is an acid albuminate containing iron and phosphorus, and is in the form of a powder. In proper cases in from ten to twenty days it causes the hæmoglobin to increase 20 to 30 per cent. (Fleischl) and produces a corresponding increase in the red blood cells. The usual dosage is from 4 to 5 drachms per day in divided doses. It is especially indicated in anæmia, chlorosis, convalescence, febrile diseases, rachitis, and, on account of its content of phosphorus, in neurasthenic conditions. Under its use not only is the condition of the blood improved, but an increase in the body weight and nourishment

is likely to take place. The author considers it an important addition to the preparations of iron already in use.—*Thérapeutische Monatshefte*, 1904, No. 3, p. 146.

The Physiological Action of Apocynum Cannabinum.—DR. HORATIO C. WOOD, JR., after an investigation of this drug, reports upon it thus: Its effects are very similar to those of digitalis. It slows the pulse and increases blood pressure, the latter effect being due to stimulation of the heart or of the vasomotor mechanism, or both. It stimulates the heart muscle directly, and, like digitalis, it causes a cessation of cardiac action through overstimulation. The author is inclined to believe that there is also an action upon the arterial walls. Studies show that the kidney circulation is diminished, due to a narrowing of the calibre of the vessels of the organ. The diuretic action of the drug is a consequence of the regulation of the circulation. The slowing of the pulse is caused by stimulation of the cardiac inhibitory centres. Like digitalis, apocynum is likely to disturb the stomach. It is possible that this effect is due to a different substance from that which causes the stimulation, and if the active principles were isolated we should have an exceedingly valuable drug.—*Therapeutic Review*, 1904, No. 3, p. 86.

The Therapeutics of Magnesium Peroxide.—MM. GILBERT and JOUNIER make the following report after a study of this agent. In doses of from 4 to 8 grains it relieves the symptoms of abnormal gastric fermentation (foul breath, regurgitation, nausea, gastric distention). In keratin-coated capsules containing from 3 to 4 grains it has proved valuable in diarrhœal conditions. Its good effect seems to be due to the liberation in the stomach or intestine of nascent oxygen.—*La presse médicale*, 1904, No. 25, p. 198.

Injections of Artificial Serum in the Vomiting of Pregnancy.—M. CONDAMIN, on the ground that the vomiting of pregnancy is due to a general toxæmia, caused, perhaps, by the extra work put upon the various organs or by the retention of toxins in the blood, has attempted to relieve the condition by injecting artificial serum. He has proceeded thus: Food, both solid and liquid, is stopped for eight or ten days. Daily rectal injections of from three to four quarts of serum are given. If these are not tolerated by the bowel a few drops of laudanum are added to the injections or they are given under the skin. In eight or ten days fluid diet is allowed, and gradually the patient returns to ordinary food, the injections being continued meanwhile. This treatment has been employed in a number of cases with beneficial results.—*Journal de médecine de Paris*, 1904, No. 7, p. 64.

Sodium Salicylate in Gonorrhœal Epididymo-orchitis.—M. CAREY reports 9 cases treated with this drug, which was administered in doses of 1 to 1½ drachms daily in solution. Only 1 patient complained of ringing in the ears, and this ceased upon diminution of the dose. The fear of evil effects upon the kidneys may be wholly disregarded. Unpleasant symptoms from the drug are likely to be rare, for the patients most subject to the inflammation in question are in the prime of life, when the emunctories are at their best. After a day or two of the treatment the symptoms are rapidly ameliorated. The pain disappears, and with it

the febrile movement and the insomnia. The tenderness is also quickly removed, the general condition is bettered, the testicle and cord return to normal size, and recovery takes place in about a week. Just as after-treatments by other methods, induration of the epididymis persists, but this seems to respond to the administration of potassium iodide. Treatment by the salicylate should not be employed as a substitute for local treatment, but in connection with it.—*Revue francaise de médecine et de chirurgie*, 1904, No. 12, p. 281.

Camphoric Acid as a Preventive of Catheter Fever.—D. A. FREUDENBURG recommends this substance in 15-grain doses, once, twice, or thrice daily, preferably in capsules, on account of its odor, commencing some days before the operation and continuing it afterward. Gastric disturbances contraindicate its use. It is believed to be a benefit in the treatment of cystitis as well.—*Gazetta degli ospedali e delle cliniche*, 1904, No. 38, p. 406.

The Treatment of Tuberculous Cystitis—M. HARTMANN recommends the following procedures in this condition: Into the empty bladder from 3 to 8 drachms, depending upon the tolerance of the organ, of iodoform 1 part, sterile liquid vaselin 20 parts are injected. The patient is instructed to watch the urine, and, upon the appearance of the oil, to stop the flow. Thus the pain caused by complete emptying of the bladder is avoided. Some individuals are able to retain the vaselin from three to six days. Reappearance of the pain shows that the vaselin has been wholly voided, and now instillations of 20 or 30 drops of iodoform 1 part, liquid guaiacol 5 parts, sterile vaselin 100 parts are given once or twice daily. At the same time capsules containing 0.15 grain of iodoform and 0.75 minim of creosote are administered. When surgical procedures, such as nephrectomy for unilateral tuberculous kidney or excision of a tuberculous ulcer of the bladder wall, are indicated they should be performed.—*Revue francaise de médecine et de chirurgie*, 1904, No. 13, p. 307.

Collargolum as a Prophylactic for Septic Processes.—DR. J. CAMERER advises prophylactic inunctions of unguentum Credé in all puerperal cases in which manual interference has been necessary or which seemed to have been rendered liable to sepsis by prolonged labor or repeated examinations. Thirty cases so treated recovered without complications. The procedure is particularly advisable in country practice, where aseptic principles are difficult to follow. The process consists in the inunction of 45 grains of the ointment twice a day for three days, using the legs and back alternately. At least thirty minutes are necessary for a proper inunction, and the rubbing should be continued until the black stain caused by the first application has entirely disappeared. —*Die Thèrapie der Gegenwart*, 1904, No. 2, p. 67.

Eucaine in Local Anæsthesia.—DR. H. C. WOOD thus describes the use of eucaine in infiltration anæsthesia. Powders containing 3 grains of beta-eucaine and 12 grains of pure sodium chloride are kept in stock. To make the solution for injection, one of these is dissolved in 3 ounces of boiling water. To this, when cool, 15 minims of 1 : 1000 adrenalin chloride are added. The whole of the solution may be used

for one infiltration if necessary, but usually less is sufficient. Even hernia operations may be done with this agent. It is necessary that a needle of platinum pointed with iridium be used, in order that it may be sterilized in flame immediately before use.—*Therapeutic Review*, 1904, No. 2, p. 52.

Potassium Permanganate in Viper Poisoning.—DOTT. ANTONIO MORI reports a successful instance, after a thorough discussion of the work done upon snake poisoning. A boy aged fourteen years was bitten upon the right hand by a viper. Ten hours afterward, while presenting to a marked degree the symptoms of poisoning, two injections of a 1 per cent. solution of potassium permanganate in the site of the wound; later intravenous injections at the elbow of the affected side were made. At four-hour intervals hypodermic injections of camphor were given, followed by as much coffee and milk as he could swallow. Recovery was complete on the ninth day.—*Gazetta degli ospedali e delle cliniche*, 1904, No. 28, p. 298.

GYNECOLOGY.

UNDER THE CHARGE OF

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ASSISTED BY

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Results of Alexander's Operation.—WALDSCHMIDT (*Zentralblatt für Gynäkologie*, 1904, No. 22) reports 185 cases from Kümmell's clinic, 101 of the patients being examined a year after the operation, with only one anatomical failure; 85 patients were entirely relieved from their former symptoms referable to the displacement; 9 women had passed through normal labors, and 10 were pregnant when examined. No case of hernia was noted. The writer insists on the limitation of the operation to cases in which the uterus is perfectly movable and the adnexa are healthy.

Hysterectomy for Obstinate Hemorrhage.—STOECKEL (*Zentralblatt für Gynäkologie*, 1904, No. 22) reports a case of endometritis in which curettement, followed by the injection of tincture of iodine and subsequently atmokausis (two minutes at 115° C.), were ineffectual. After prolonged hemorrhages the uterus was extirpated, when it was found that the diseased mucosa in both cornua had not been affected by the previous treatment.

Hysterectomy for Cancer of the Corpus Uteri.—BAEKER (*Zentralblatt für Gynäkologie*, 1904, No. 22) showed at the Hungarian Medical Association two uteri which he had extirpated for obstinate hemor-

rhage that had resisted repeated curetting. In one instance the patient had been curetted twenty times (!), the microscopic diagnosis being always "glandular endometritis," until the last examination pointed to probable adenocarcinoma. The writer believes that these cases illustrate forcibly the theory that endometritis is an important factor in the etiology of cancer. [Every gynecologist meets with similar cases in which the clinical symptoms point so strongly to the presence of malignant disease that he feels qualified in performing hysterectomy, in spite of the favorable prognosis of the pathologist.—H. C. C.]

Indications for Vaginal Section.—FOURNIER (*La Gynécologie*, April, 1904) limits posterior colpotomy to cases in which there is a distinct swelling in the cul-de-sac, associated with fever. He regards it as simply a palliative measure for the evacuation of pus, and that it should be understood in every case that the *cause* of the trouble has not been removed, so that a radical operation will probably be necessary later.

Indications for Splenectomy.—JORDAN (*Berliner klinische Wochenschrift*, 1903, No. 52) believes that with improved technique and statistics the indications for this operation have been unduly extended.

Rupture of the spleen is a positive indication for extirpation, over thirty successful cases having been reported. It may become necessary even in the case of a small wound, especially if infected.

Simple and echinococcus cysts justify splenectomy, eight cases of the former having been reported, with no mortality, and seventeen of the latter, with two deaths.

Four successful cases of extirpation of the organ for sarcoma, one for lymphosarcoma, and one for angioma are on record, but in all except one case of sarcoma there was a recurrence of the disease.

Leukæmia and pseudoleukæmia, in the author's opinion, are contraindications to operation, since every case thus treated has terminated fatally. Spleens enlarged from malaria and chronic hyperplasia can be successfully extirpated; also cases of hyperplasia in connection with cirrhosis of the liver (seventeen recorded operations, with three deaths).

Movable spleens, being usually diseased, should be removed. Splenopexy is to be considered. A rare indication for splenectomy is necrosis and perisplenitic abscesses, seven successful cases of which have been reported.

Lymphatic Infection in Cancer of the Uterus.—MME. ALTRAMARE (*Annales de Gynéco'ogie et d'Obstétrique*, June, 1904), after a review of the writings of those who favor radical abdominal hysterectomy, principally on the ground that infected lymph nodes and periuterine tissues can be more thoroughly removed, concludes that logically the only real radical operation should include removal of the entire uterus, vagina, both broad ligaments, and ureters, and all the lymphatics as high as the iliac glands.

Statistics show that involvement of the lymph nodes occurs in only 20 per cent. of cases of cancer of the uterus, and that recurrences are nearly always local, occurring in the pelvic tissues, the bladder, or vaginal vault. The writer denies that the permanent results have been any better since the adoption of the radical operation. She concludes that

a systematic search for lymph nodes during an operation for extirpation of the cancerous uterus introduces an unnecessary complication and renders the prognosis less favorable, since the glands are often not found, and when removed the disease recurs in the broad ligaments the same as after vaginal hysterectomy. She believes that an improvement in the statistics of hysterectomy for cancer of the uterus is to be expected rather from early recognition of cancer, than from illusive attempts to remove all the outlying foci in more advanced disease.

Action of Caustics on the Endometrium.—RIELAENDER (*Zentralblatt für Gynäkologie*, 1904, No. 26) studied the action of 30 and 50 per cent. alcoholic formalin solutions, strong nitrate of silver, and tincture of iodine by introducing these drugs into the uterine cavity on an applicator twenty-four hours before extirpation of the uterus. The operation was performed for the relief of obstinate hemorrhages. The writer concludes that alcoholic solutions of caustics are preferable for intrauterine use, because they penetrate more deeply into the tissues. Applications are better than injections, as there is no risk of entering the tubes. Within twenty-four hours (!) after the application of a 30 per cent. alcoholic solution of formalin a slough was cast off and regeneration of the mucosa had begun.

[It is difficult to reconcile these conclusions with those of other competent observers who claim that several weeks elapse before regeneration of the endometrum is completed.—H. C. C.]

Deciduoma Malignum.—BAROZZI (*La Gynécologie*, June, 1904) contributes an article on this subject, with exhaustive bibliography, no new conclusions being reached. After an historical review, he discusses the pathological anatomy, stating that in the majority of the reported cases the mucous membrane is primarily involved, usually near the fundus, but the disease extends rapidly to the uterine muscle. The uterus is not enlarged until the later stages, and rarely reaches the size of the fetal head at term. Contrary to the conditions in cancer, in deciduoma metastases are so frequent as to form a distinctive feature of the disease; the lungs are their favorite seat, so that the pulmonary symptoms may be the most prominent. Metastatic nodules in the vagina are next in order of frequency, though any organ (and even the nervous system) may be involved. This tendency to metastasis is explained by the early destruction of the vessel walls by the plasmodial masses or syncytial cells, and their entrance into the blood.

Two varieties of deciduoma are recognized histologically, the typical characterized by the presence of ramifying plasmodial bodies, between which are nodules composed of mononucleated cells, and the atypical, in which small groups and isolated plasmodial bodies are seen. A mixed type has been described. It has not yet been determined positively whether one variety is more virulent than the other.

The onset of the disease may be so insidious that the results of metastasis may be apparent before the local condition is suspected. In most cases, however, the history of previous pregnancy and obstinate hemorrhages, with rapid decline in the general health, point to the probable diagnosis, which is confirmed by the removal of fragments of the neoplasm. Deciduoma usually attacks multiparæ between the ages of twenty and thirty years, the symptoms appearing between two

and four months after labor or abortion, though there are wide variations. The writer agrees with Durante in casting doubt upon cases in which from one to two years have elapsed since previous pregnancy, as an early abortion may have passed unnoticed, or the patient may have long had a placental polypus.

The prognosis is absolutely bad, for without operation the disease terminates fatally in from one to six months, though a few cases have been reported in which the patient survived for a year or more. The only known prophylaxis is to remove every bit of retained placental tissue after labor and abortion, and especially placental and hydatiform moles. If hemorrhages persist after thorough curettement, even though no neoplasm can be found, the writer believes that hysterectomy should be performed without delay. The surgeon should not be thrown off his guard by believing that the symptom is due to a "hemorrhagic endometritis." The only possibility of obtaining a cure lies in early operation, before metastases have occurred. Ladinski's statistics (124 operations, with 51 cures) are imperfect, since later writers have reported nine operations in which the patients were free from recurrence from one to six years afterward.

Recurrent Fibroma of the Uterus.—GROENZDER (*Roussky Vratch; La Gynécologie*, June, 1904), while admitting that so-called "recurrent fibroma" is really sarcoma, contends that it is sarcoma of a peculiar type. He reports a case of persistent metrorrhagia and abdominal pain in a woman, aged forty-four years, from whom a necrotic intrauterine polypus was removed, presenting no microscopic evidence of malignancy. Ten months later a similar polypus was removed, metrorrhagia having returned six months after the former operation. The bleeding continued, and as hysterectomy was rejected, the operator was obliged to content himself with the excision of a third polypus, which differed histologically from the other two only in containing groups of suspicious ovoid cells. Finally, two years after the first operation, the patient re-entered the hospital with her uterus enlarged to the size of the fetal head at term. It was removed by laparotomy, and the patient was not seen for six months, when she returned with recurrence in the lumbar glands, and eventually succumbed.

On section of the uterus the endometrium was found to be replaced by soft granulation tissue. The uterine muscle around the tumor showed fatty degeneration and necrosis of the muscle fibres. The structure of the tumor presented somewhat the same appearance. The writer believes that the polypi first removed were sarcomata, their true character having been overlooked.

Follicular Carcinoma of the Ovary.—VOIGT (*Archiv für Gynäkologie*, Band lxx., Heft 1), in describing a case of his own, concludes that it originated not in the primordial follicles, but in the superficial germinal epithelium by the ingrowth of follicular bodies, some of which formed pseudomucin cystomata and the other adenocarcinoma. He reviews Kossmann's theory that papillary as well as serous and simple adenocystomata of the ovary are developed from isolated masses of Müller's epithelium derived from the superficial layer. Just like the epithelium of Müller's ducts in the cervix, the same cells in the ovary may assume different characters.

OPHTHALMOLOGY.

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Ocular Complications of Bright's Disease —STRICKER, of Cincinnati (*Journal of the American Medical Association*, February 20, 1904), presents a study of these conditions, and reports 16 cases. All but 4 of these were cases of some form of neuritis or neuroretinitis; the 4 exceptions were: 1 venous thrombosis, 2 uræmic amaurosis, and 1 keratitis, in all probability a general uveitis. Of these cases 2 occurred during pregnancy as acute Bright's disease. Both are living, in 1 case with vision greatly impaired. Four were cases of chronic parenchymatous nephritis following acute diseases; all of these died. Ten were cases of chronic interstitial nephritis, 7 of which p oved fata'. He sums up in the following conclusions: 1. There are no ocular complications pathognomonic of Bright's disease. 2. The characteristic fundus picture—hemorrhages, areas of degeneration, white sp ashes in the macular region—may not be present; one may meet with any of the many manifestations of vascular or retinal inflammation due to toxins. 3. Ocular complications occur in only a mall percentage of Bright's disease, partly because lesions not causing functional disturbances are apt to be overlooked. 4. All the ocular complications are the result of a chronic uræmia. 5. The ocular lesions of Bright's disease are of most serious prognostic import as regards the life of the patient. 6. The prognosis is better in the acute form conditions, though the vision remains greatly impaired. 7. The amount of urea excreted in twenty-four hours is the best indication of the early or immediate fatal outcome of the case. 8. In pregnancy cases a low excretion of urea should call for immediate interference to save the eyesight, as well as the life of the mother. 9. In the choroidal and retinal changes the writer has found the amount of urea below the normal. He regards its retention or that of other excrementitious substances in the blood due to faulty kidney action as directly responsible for the inflammatory or degenerative changes.

Certain Cases of Asthenopia and Eye-strain which are Independent of Refractive Error and Muscular Imbalance.—DE SCHWEINITZ (*University of Pennsylvania Medical Bulletin*, June, 1904), after referring to the universally known ill-effects of anomalies of refraction, accommodation and motility of th eyes, comprising, indeed, fully 75 per cent. of ocular disorders, and whose influence is also felt in parts of the system remote from the eyes, observes that causes of eye-strain unrelated to the e anomalies have not unnatural y failed, perhaps, to receive the attention they deserve, although this side of the question has not been

entirely neglected. The writer proceeds to give a résumé of personal experience in this matter. These embrace: Simulation of eye-strain and asthenopia by symptoms depending upon the lithæmic state (the serious ocular disorders which may result from this condition, for example, various types of keratitis, iritis, etc., are not now under consideration). Some of the cases to which reference is made are as follows: Itching, burning, or formication of the eyelid margins. Œdema of the eyelids, tender spots in the ciliary body, wi h pinpoint ocular pain, foreign body sensations in the eye, subnormal amplitude of accommodation. For many of these conditions glasses are not a panacea. They are to be examined with the aid of the advanced physiological chemistry and treated in accordance with the results so obtained.

Glaucoma and Glaucoma Theories.—PATTERSON, Edinburgh (*Medical Press*, February 17, 1904), dealing first with the normal condition, pointed out that the aqueous humor was secreted by the epithelium in the ciliary region and eliminated by the filtration angle, and, to a less extent, by the vessels of the iris. The exact channels of outflow are determined by the elimination of Indian ink after injection into the vitreous. Leber's estimate that the fluid in the anterior chamber was renewed every forty minutes seems too high. There is no appearance of current in the anterior chamber, so that outflow must be very gradual. The intraocular pressure is intermediate between the arterial and venous capillaries, about 25 mm. Hg., subject to slight variations and not affected by accommodation. It can never, of course, exceed that of the arteries supplying the eyeball.

Turning to glaucoma, this was defined as a state of increased intraocular tension. Part of our lack of knowledge of pathology is due to the fact that attempts to produce it artificially in animals have met with little success. Another great obstacle is the fact that eyes were not enucleated at an early stage, but only when secondary changes had set in. The morbid appearances of such eyes are now perfectly well known, but it is impossible to say which of these changes is the primary cause of the disease.

A short discussion of the various theories of glaucoma follows. Von Graefe and Donders thought it was due to hypersecretion; Knies had ascribed it to a blocking of the filtration angle by adhesive inflammation of the tissues in that region; while Weber thought that a similar blockage took place in consequence of swelling of the ciliary body. While the lesion described by Knies was of the greatest importance, it could only be regarded as secondary, since it was absent in early cases of acute glaucoma. Priestley Smith's view, that, especially in hypermetropic eyes, the circumlental space becomes narrowed by the growth of the lens, which latter might be completely obliterated by swelling of the ciliary processes, pressing the root of the iris forward and occluding the filtration angle. There was, however, no direct evidence of this hypothesis. The theories of Panas, Abadie, and others were passed in review and shown to be untenable or inadequate. Stress was laid on the frequency with which chronic glaucoma was associated with general vascular changes, and while some forms of eye (hyperopic) were predisposed to glaucoma, others (myopic) were not. Careful examination of the circulatory system by modern instruments for investigating blood pressure might throw some light on the pathology of the subject. Little more

was to be gained by examination of old glaucomatous eyes or experiments on animals, but if, as he was informed, that it was true that domestic pets kept under highly artificial conditions—*e. g.*, pampered lap-dogs—were occasionally the subjects of glaucoma, it might at some time be possible to get an eye in the early stage from this source.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.,
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Chronic Coryza.—Dr. L. Jacquet, of Paris, contributes a communication (*Annales des Maladies de l'Oreille, du Larynx*, etc., March, 1904) concerning an albuminuric patient in whom an attack of severe and obstinate coryza was relieved during treatment of the albuminuria by omitting salt from the diet. On experimentation he found personally that by diminishing the salt in his own food he could quiet a coryzaic condition to which he is subject. He, therefore, suggests that this treatment be essayed for ordinary chronic coryza.

Hay Fever.—In a paper on "The Relation of the Chemistry of the Saliva and Nasal Secretions to Diseases of the Mucous Membrane of the Mouth and Upper Respiratory Tract, with Special Reference to Hay Fever," and read before the Section on Laryngology at the recent meeting of the American Medical Association (*American Medicine*, June 18, 1904), Dr. D. Braden Kyle, of Philadelphia, expressed his belief in the importance of the consideration of the individual character of these secretions which, under certain conditions, are irritating, while non-irritating in others. He advises treatment directed toward rectifying the pathologic conditions of the secretions to be begun several weeks before the usual time for the hay fever attack to come on in individuals who have been chronically susceptible. In acute attacks the same line of treatment is to be carried out, though more vigorously, the secretions being rapidly shifted from acid to alkaline, or *vice versa*. Dr. Kyle reports 80 per cent. to 90 per cent. of cures in patients treated on this basis.

Reflex Apnœa and Cardiac Inhibition in Operations upon the Respiratory Tract.—In a paper on this subject read at the recent meeting of the American Medical Association by Drs. William Harmar Good and W. G. B. Harland, of Philadelphia (*American Medicine*, June 11, 1904), and based especially on observations during adenoid operations and during intubation in which cases of instant death are on record, they conclude that the origin of reflex apnœa and cardiac inhibition is through the medulla by irritation of trifacial and sensory

branches of the vagus; that inhibition may be caused by irritation of the mucosa of the nose, rhinopharynx, larynx, and lungs; that obstruction to respiration is indicated by cyanosis and full pulse, while reflex inhibition produces pallor and slow, weak pulse.

Infections of the Lymph Glands of the Mouth and Throat.—Dr. Robert T. Morris, of New York, read a paper on this subject before the First District Society of the State of New York last December (*The Dental Cosmos*, June, 1904). He calls attention to Ludwig's angina and other affections proceeding from infections in the mouth. He discusses the methods of treatment that should be instituted from this point of view.

Melanotic Sarcoma of the Soft Palate.—At a recent meeting of the Laryngological Society of London (*Journal of Laryngology, Rhinology, and Otology*, June, 1904), Dr. J. B. Ball showed a case of melanotic sarcoma of the soft palate in a man, aged fifty-three years. The patient had first noticed some black patches on the palate two years previously. Some seven or eight months ago a growth commenced on the soft palate, but as it gave no inconvenience little notice of it was taken until three weeks ago, when it bled, and he then showed it to his doctor. A dark-looking, flattened, somewhat mushroom-like growth covered an area about the size of a shilling on the middle of the soft palate. There were numerous black patches on the hard and soft palate and on the upper gums. There was some slight glandular enlargement under the chin near the middle line. The patient had lost about a stone in weight during the last twelve months.

Pachydermia Laryngis.—In discussing a laryngoscopic image of a woman, aged forty-three years, shown to the Laryngological Society of London by Mr. de Santi (*Journal of Laryngology, Rhinology, and Otology*, June, 1904), the President, Dr. McBride, called attention to the fact that the pachydermia involved the anterior commissure as well as the interarytenoid space and vocal processes to which this lesion is confined in most instances.

Treatment of Ulcerated Epitheliomas of the Upper Air-passages by Applications of Adrenalin.—Dr. Georges Mahu reports (*Annales des Maladies de l'Oreille, du Larynx*, etc., March, 1904) a number of instances of epitheliomas of the tongue, pharynx, larynx, and other regions very much benefited by applications of adrenalin, 1:1000. Hemorrhages seemed very easily arrested, and the patients improved very much for the time being. Attempts to hasten matters by injections of the solution were injurious, and led to the development of new vegetations.

Removal of Pin from the Lung through the Natural Passages.—Dr. E. Fletcher Ingals reports (*Journal of the American Medical Association*, April 30, 1904) a case in which, with the aid of a Killian bronchoscope and tube forceps, he was able to remove from one of the divisions of the right bronchus, where it had been detected by radiography the day previous, a large glass-headed pin which had been inhaled into the windpipe of a young woman nearly a year before.

DERMATOLOGY.

UNDER THE CHARGE OF

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The Tuberculous Nature of Angiokeratoma.—PAUTRIER (*Archiv für Dermatologie und Syphilis*, Band lxix., Heft 1 and 2) believes that angiokeratoma should be placed among the tuberculous affections of the skin, and presents a number of histological facts in support of this view of its etiology. The occurrence of this affection in those who present certain and well-marked evidence of tuberculous disease and its association with other tuberculous eruptions are adduced as clinical evidence of the great probability of its tuberculous character. After referring to a number of cases reported by other observers in which angiokeratoma was associated with other well-defined tuberculous affections, he reports the case of a young woman under his own observation, in whom angiokeratoma coexisted with typical lupus pernio and tuberculosis of the lungs. The father of the patient had a typical lupus erythematosus of the ears, and a maternal uncle and an aunt had died of tuberculosis of the lungs.

The histological changes correspond to those found in the tuberculides, more especially to the necrotic tuberculides.

A Hyperkeratosic Exanthem in Severe Gonorrhœal Infection.—BAERMANN (*Archiv für Dermatologie und Syphilis*, Band lxix., Heft 3) reports in detail 2 cases of a rare eruption associated with severe general gonorrhœal infection. The eruption was a polymorphous one and occurred under two forms: 1. Disseminated lesions distributed over the whole body. 2. Aggregated lesions upon the hands and feet, more especially the fingers and toes. In the disseminated variety scaly lesions seated upon a non-inflammatory base were scattered over the entire body, more particularly the extremities, rarely upon the scalp, and almost never upon the face. The eruption was composed of scales much like the thick scales seen in psoriasis complicated with a local seborrhœa; it was infrequently preceded by a vesicular stage. Very often, especially in the older and larger lesions, the scales were lamellated like the shell of an oyster, and occasionally they formed cone-like structures. The color was a dirty-yellow, the lesions showed a certain translucency, and they sometimes looked as if varnished. The scales were strongly adherent, and when forcibly removed, showed a dry or moist, red, papillomatous base. The form localized upon the hands and feet was much more common than the disseminated form, and presented quite a different picture. Occasionally a few small lesions like those already described were found upon the hands and feet surrounded by a callus-like thickening. More commonly the horny layer of the

palms and soles was thickened diffusely, was of a dirty, yellowish-brown color, and was marked, more especially on the borders, by deep furrows. Upon such a base were situated discrete or confluent, moderately smooth or deeply fissured, cone-like prominences. Points of pressure upon the palms and soles were especially affected, as well as the nails and the nail-folds, particularly of the toes, the nails becoming opaque and brittle. The nails in some instances were lost completely, the nail-bed being covered only with a thin, oozing layer of epidermis. Oftentimes these lesions occurred in plaques upon the lower extremities, especially on surfaces exposed to friction or in contact. Those extremities were most affected in which, owing to disease of the joints, a considerable degree of muscular atrophy had taken place. The microscopic changes consisted of a moderate dilatation of the cutaneous vessels, which were surrounded by an abundant infiltration of leukocytes. In the deeper layers of the epithelium were numerous migratory cells, and the papillæ showed proliferation. The horny deposits consisted of incompletely cornified, parakeratotic cells with still demonstrable nuclei. Foci of softening were present in the horny cones and in the thicker scales. Gonococci were never found in the eruption.

Pityriasis Rosea.—HARVEY P. TOWLE (*Journal of Cutaneous Diseases*, April, 1904) considers this disease in the light of reported cases and his own experience, and concludes, from an analysis of a series of 202 cases, that the disease occurs in two forms, the macular and the circinate, with about equal frequency. It occurs most often on the trunk and the upper parts of the extremities, but occasionally is confined to one part. It is most common in the autumn, and is met with more often in women than in men. It may occur at any age, although most frequent between twenty and thirty years. As a rule, there are no prodromata or accompanying disturbance of the general health. Itching may or may not be present. Histologically, the chief changes are in the cutis.

Acne Rosacea and Its Treatment.—A. D. MEWBORN (*Journal of Cutaneous Diseases*, April, 1904, p 192) calls attention to the value of the so-called scaling treatment by such remedies as a solution of resorcin, 10; sulphur, 10, and tincture of soft soap, 40, used for three successive nights during each week. A case is given in which the use of the high-frequency current and the Roentgen ray alone, used for several months, had failed, but was cured by opening the pustules with a lancet and using the scaling treatment referred to. He thinks the Roentgen rays should not be employed until the milder forms of treatment have failed.

Treatment of Ringworm with Chrysarobin.—HODARA (*Jour. des mal. Cut. et Syph.*, August, 1903) recommends a solution of equal parts of glycerin and chloroform containing from 5 to 10 per cent. of chrysarobin, to be applied daily after shaving of the scalp, continued until œdema and slight erythema are produced. Four or five months are required to effect a cure.

Pityriasis Rubra (Hebra).—TSCHLENOW (*Arch. für Derm. und Syph.*, Band lxiv. Heft 1) considers the following as the more important pathognomonic symptoms of this rare disease. Loosening of the corneous layer

in the form of small lamella and the presence of nucleated cells, more or less disappearance of the corneous layer, thickening of the mucous layer, followed by thinning of the same, disappearance of pigment in the basal stratum, augmentation of the connective tissue, bloodvessel changes, and atrophy of the skin. He distinguishes clearly between this disease and dermatitis exfoliativa. He deplores as unscientific Brocq's group of pityriasis rubra and Besnier's erythrodermies exfoliantes.

The Action of Formalin upon the Fungus of Favus.—BOGROW and SCHARKEWITSCH-SCHARSCHINSKY (*Dermatologische Zeitschrift*, Band xi., Heft 5), as the result of experimental investigations with formalin in favus, conclude as follows: The 5 per cent. watery solution of formalin kills the *achorion*, cultivated from epilated hairs after the method of Plaut, in twenty minutes, and may act still more rapidly. An increase in mechanical hindrances, such as particles of the nutrient media clinging to the culture or thickness of the mycelium, may completely annul the action of watery solutions. Those parts of the hair which are in the skin are inaccessible to solutions of formalin in water, probably on account of the fat in the hair. The employment of formalin solutions does not facilitate the treatment of favus. As to the effect of spirituous solutions and formalin vapor upon the *achorion*, further observations are desirable.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Ankylostomiasis (Uncinariasis) not Essentially a Miners' Disease.—But a few years ago ankylostomiasis was regarded as a parasitic disease peculiar to certain localities and associated especially with coal-mining and other occupations carried on underground, and the vehicle of infection was thought to be polluted water. In 1902 DR. CHARLES WARDELL STILES (*Public Health Reports*, October 24, 1902) discovered that in some parts of the South it is the most common disease of man, and that the infection is less severe and less common in the mining districts than on the farms and plantations of the sand district. HARRIS (*American Medicine*, November 15, 1902) and other Southern observers confirmed the conclusions of Stiles, by whom, also, it was pointed out that the dissemination of the parasite is not due to polluted water, but to polluted soil; and BAKER (*British Medical Journal*, March 28, 1903) asserted that the embryos cannot live in water. Now, the disease has been found to exist in many districts of Europe where it never before was suspected, and it would appear that it is very widely disseminated and has been for a long time. With regard to its being in Europe essentially a miners' disease, the observations of the DRS. IBERER (*Münchener*

medicinische Wochenschrift, 1903, No. 23, p. 992) are of interest, since they are in full accord with the findings of American investigators. They are of the opinion that sunlight not only is not harmful, but distinctly favorable to the development of the larvæ. On the other hand, water at 44° F. to 61° F. kills the eggs, embryos, and larvæ. They have had occasion to examine large numbers of peasant lads who have never worked in the mines and yet have yielded, in very many instances, large numbers of the parasites. Hence they conclude that the disease is endemic on the farms. Even when the parasites were found in great numbers the subjects were often neither poor in blood nor otherwise ailing. Many of the lads who went away for their three years' military duty returned, at the expiration of their terms of service, still infested, but with no history of having suffered in any way in consequence. Of the miners examined, no less than 94 per cent. were found to be infested, but not more than one in four was ever incapacitated, even temporarily.

Meat Poisoning and Paratyphoid.—An outbreak of meat poisoning in Düsseldorf, in which fifty-seven persons fell sick during a period of six days after eating chopped horsemeat, has led to interesting investigations concerning the bacteria that have been demonstrated as the exciting causes of this and other outbreaks of the past. In this outbreak one of the victims ate the meat in the form of boiled sausage, three ate it stewed, and the rest ate it raw. The meat was unobjectionable as to taste, odor, and appearance; it was derived from different animals, but was all from one shop. It is an interesting fact that the butcher who minced and sold the meat bought part of it, a hindquarter, of another butcher, who sold the other three quarters to customers not one of whom was made sick. In the great majority of those who were attacked, the symptoms were vomiting, diarrhœa, and vertigo; thirty-one were sick enough to need a physician, not a few were incapacitated for a long time, and one, a boy of nine years, died. From the spleen of this victim a short bacillus was isolated that proved to be very virulent for mice and guinea-pigs, less so for rats and rabbits, and not at all for dogs and cats. Boiled cultures were not pathogenic for guinea-pigs and rats, but were for mice. This organism has been studied carefully by Dr. H. Trautmann (*Zeitschrift für Hygiene und Infectionskrankheiten*, xlv., p. 139) and compared with *B. friedebergensis* (Gaffky and Paak), *B. enteritidis* (Gärtner), *B. breslaviensis* (Kaensche), *B. morsulensis* (van Ermengern), and the bacteria of other outbreaks of meat poisoning investigated by Fischer, Abel, Günther and others; also with Basenau's *B. bovis morbificans*, Brion-Kayser's paratyphoid bacillus of type A. and Schottmüller's, Hünerman's, and Conradi, Drigalski and Jürgens' paratyphoid bacilli of type B. He comes to the conclusion that these organisms, while presenting slight differences in form, size, staining properties, motility, and growth on culture media, show no fundamental difference and are merely variations of one and the same organism. In a second communication (*Ibid.*, xlvi., p. 68) he cites certain variations in the kind and severity of symptoms and in the order of their appearance are dependent upon these slight variations in the bacterial races and upon the degree of virulence and individual susceptibility. In meat poisoning the initial disease is an animal disease, and when the animal is killed on account of sickness and the meat is sold as food for man, containing the pathogenic organisms and their poisonous products, it may cause after some hours, or more commonly some

days, a train of symptoms of varying severity. It may result in violent gastroenteric symptoms with consequent expulsion of the offending material, or absorption of the poison may occur and produce general systemic disturbance, the severity of which varies according to dose and individual peculiarity. In the lesser cases we may observe, in addition to vomiting and diarrhœa, abdominal pain, headache, backache, dizziness, general malaise, skin eruptions, and the like; in the more severe cases, unconsciousness, delirium, and the choleraic condition. Many cases of meat poisoning can hardly be distinguished from paratyphoid, and severe cases are sometimes difficult to distinguish from real typhoid. Indeed, many outbreaks of meat poisoning have been diagnosed incorrectly as typhoid. Trautmann believes that the typical meat poisoning is a most acute, and the paratyphoid condition is more a subacute, manifestation of an etiologically similar disturbance. Since the urine and feces of the sick animals and of paratyphoid subjects can reach water supplies equally well with typhoid excreta, the mode of infection and spread may be similar.

Investigation of the Düsseldorf outbreak showed among other things the following interesting facts: The premises of the butcher who sold the meat, and his tools, including the hashing machine, were in a condition of great uncleanliness. The hindquarter which he obtained elsewhere made people ill, although the rest of the carcass caused no trouble; this hindquarter was not mixed with other meat, and it was probably infected by the dirty implements.

Fleas and Plague.—Discussing a criticism of a report of an outbreak of plague that in respect to transmission by fleas "the weakest link in the chain is in reality the absence of any proof that the rat flea is under any circumstances so commonly parasitic to human beings as to become an etiological factor of any epidemiological significance whatever," Dr. J. S. C. Elkington, of Hobart, Tasmania (*Public Health*, July, 1904, p. 645), points out that the very marked differences in structure and habits shown by the different species and genera of fleas that infest rats make it as unscientific to speak of the rat flea without qualification in connection with plague as to speak of the mosquito in general as the conveyor of malaria. In Bombay and in certain parts of Australia, the most common rat flea is a pulex that closely resembles that which infests man, while in England it is one of another genus (Ceratophyllus) and differs widely from the two above mentioned. The rat flea of New South Wales, Victoria, and West Australia resembles closely the *Pulex pallidus* of Bombay, but the common rat flea of Tasmania and New Zealand differs widely from either, as does that of England. The rat flea (pulex) of Bombay and Victoria will under certain conditions feed vigorously on man, but the Ceratophyllus and Typhlopsilla genera can be induced to do so only with great difficulty, if at all, and to this fact may be due Galli-Valerio's negative results. The flea that infests man may be starved into feeding also on rats. Having in mind the following facts, it appears that the flea cannot be dismissed offhand as an innocent agent in connection with plague: 1. Fleas of certain species may carry virulent plague bacilli several days, and the bacilli can multiply without harming the insect. 2. The common rat flea of certain localities wherein rat plague is associated habitually with human plague is a pulex closely resembling the *Pulex irritans* of man, while that of certain other localities wherein rat plague is not so associated

belongs to another genus or other genera, differing widely in structure and apparently also in habits. 3. The inoculation of blood containing plague bacilli or of the bacilli separated from the blood of either rat or man will produce plague in man. 4. The rat pulices of Bombay and of certain parts of Australia, at least, will feed on man when hungry, and the *Pulex irritans* will similarly feed on rats. 5. The plague bacillus probably exists in the blood of every fatal human case at some time and certainly does so in great numbers in the septicæmic form of the disease. It also exists in great numbers, as a rule, in the blood of plague-stricken rats.

The Possibility of Tubercular Infection through Books from Public and Circulating Libraries.—The report that a number of clerks in a public office in this country had become tuberculous through handling books that had been infected by another who had had the habit of wetting his fingers with saliva when turning the leaves suggested to Dr. I. Mitulescu (*Zeitschrift für Hygiene und Infectionskrankheiten*, xliv., p. 397) an examination of popular library books, which, passing from hand to hand, must become exposed to infection from tuberculous readers. Thirty-seven books and periodicals, chiefly novels and stories, from three to six years old and all very dirty, especially on the edges and corners, constituted the first lot examined. The results of animal experimentation conducted on the usual lines demonstrated the presence of virulent tubercle bacilli in more than a third of the books; but the development of the disease was very slow and the amount of general infection was small, which facts suggest only moderate virulence and limited numbers of bacilli. A second lot of 60 books, including 20 that had been two years in use, 20 one year, and 20 six months failed to yield any tubercle bacilli. Of the 120 guinea-pigs employed, 31 died of various acute infections, but the remaining 89 after being kept from three and a half to four months were killed and examined, but showed no evidence of tubercular infection. The books of the first lot that gave positive results were old and dirty; the leaves of some of them stuck together. The other books were comparatively clean, having been much less long in service. The difference in infectivity (for both lots had doubtless been handled by consumptives) probably resides in the fact that tubercle bacilli will live longer in the moist dirt of old books than on the fresh, clean surface of new ones, on which the sputum is more easily and completely dried. It is not to be assumed, however, that comparatively new books may not convey infection, for they may be read by many and pass quickly from one to another; but the danger is greater with old books well encrusted with the protective dirt. The public should be taught not to wet the leaves of books while reading, and one should always wash the hands carefully after contact with books whose history is not known.

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